LETTERS

Axillary hyperhidrosis treated with botulinum toxin A exotoxin

To the Editor

Axillary hyperhidrosis is a common disorder of sweating. In severe cases, profuse axillary sweating leads to skin maceration that may cause secondary infections. Pathophysiology of sweating is complex.[1,2] The eccrine glands play an important part in thermoregulation and are located throughout the body, but are concentrated in the palms, soles and axillae.[1] The eccrine glands receive sympathetic innervation, and the neurotransmitter involved is acetylcholine.[2] Eccrine sweat glands have been shown to be stimulated by cholinergic as well as adrenergic agonists.[3] Systemic anticholinergic agents frequently have unacceptable side-effects. Surgical treatments, such as transthoracic sympathectomy often fail to cure axillary hyperhidrosis, and complications may include pneumothorax and compensatory hyperhidrosis in other parts of the body.[4]

Recent studies have demonstrated a reduction in axillary sweating production with the intradermal use of botulinum toxin A (BTX-A).[5,6] We have studied the long-term therapeutic effects of BTX-A in patients with axillary hyperhidrosis. We treated seven adult patients (five men and two women; mean ± SD age, 34.2 ± 10.4) with severe axillary hyperhidrosis that was unresponsive to any prior therapies. The duration of axillary hyperhidrosis was 10.7 ± 3.5 (mean ± SD) years. The dermatological and neurological examination of all patients was normal except for axillary hyperhidrosis. There were no other disorders that could cause secondary hyperhidrosis, such as obesity, menopause, drug use, endocrine disorders or neurological condition in any of the patients. The patients were instructed about the procedure upon their written informed consent. Before and 2 weeks and 4, 8 and 12 months after the BTX-A injections, the area of hyperhidrosis was visualized by Minor's iodine-starch test (fig. 1). In this test, an iodine solution (2 g of iodine in 10 mL of castor oil and alcohol to 100 mL) was painted over the area of the skin to be tested. After it had dried, fine rice starch powder was applied. Skin causes the mixture to turn dark blue–black. Before and 4, 8 and 12 months after BTX-A injection, the amount of axillary sweating was collected during a 1-min period after the hyperhidrotic area was blotted dry and then brought into contact with filter paper. The hyperhidrotic areas were identified with the iodine-starch test and subdivided into squares of 2 × 2 cm. Lyophilized BTX-A [Botox, Allergan, Inc., Irvine, CA, USA; 100 mouse units (MU)] was diluted in 5 mL of sterile 0.9% saline. Portions of 0.15 mL (3 MU) were distributed intracutaneously over an area of 4 cm^2 from a single insertion.

All the patients noticed a significant reduction in axillary sweating 3 days after injection. The area and the amount of the sweating was documented by Minor's iodine-starch test and filter paper. Quantitatively, sweating declined significantly from 98 ± 13 mg/min before the BTX-A injection to 42 ± 9 in the fourth month, and was 50 ± 6, 75 ± 4 mg/min at the end of the eighth and 12th months after injection, respectively ($P < 0.001$, *t*-test) (fig. 2). The BTX-A injection was well tolerated except for moderate pain. Treatment of axillary hyperhidrosis with BTX-A is an easy procedure, and appears to be safe, simple and also very effective. Another major advantage is the localized effect of compensatory hyperhidrosis, which has never been reported elsewhere.[5–7] Recent studies have demonstrated a reduction in axillary sweating in patients with focal hyperhidrosis following chemodenervation with BTX-A.[5–7] The dose-related clinical effect of BTX-A appears to be longer-lasting when applied to sweat glands.[5,8] Injection of 50 U per axilla resulted in total anhidrosis, which persisted for 8 months. With 30 U, the axillary sweating was substantially reduced, and the effects wore off in 6 months. There were no effects observed with an injection of 20 U.[8] With an injection of

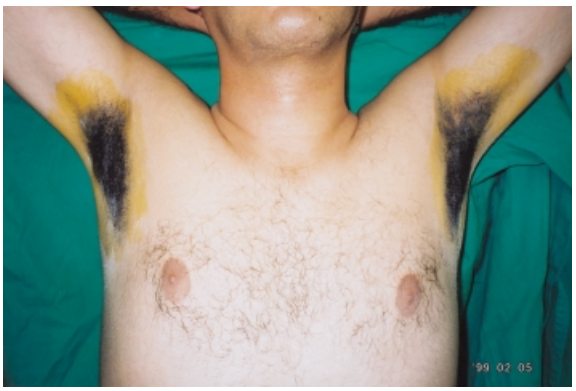

fig. 1 Staining of hyperhidrotic areas using Minor's iodine-starch test.

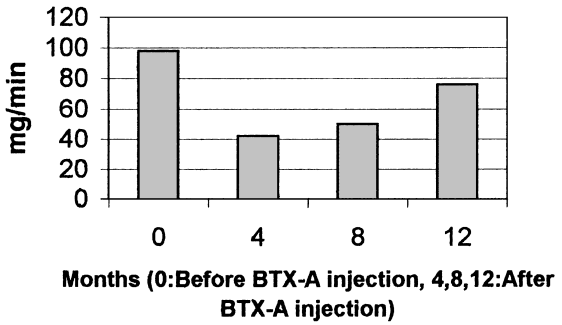

fig. 2 Quantity of the sweating according to the months (mg/min).

3 MU BTX-A into squares of 4 cm^2 at the axillary hyperhidrotic area, the effects of hyperhidrosis were observed within the follow-up period for up to 5 months.[5] The treatment of axillary hyperhidrosis with high-dose BTX-A seems to be as safe as low-dose BTX-A and has a lower rate of relapse.[9] The results of the present study were similar to those in other studies. BTX-A is a potent but very fragile toxin; therefore, care should be taken not to agitate the solution during the dilution and filling of the syringe. The different results of the duration effects of BTX-A with the same doses may be due to an inappropriate dilution method. The effects of BTX-A do not disappear completely at the end of 1 year. The optimal dose and the lowest dose for the treatment of axillary hyperhidrosis still needs to be defined to minimize dose-related side-effects, to lower the costs of treatment and to reduce the risk of antibody formation.[4,10]

Owing to the effects of factors such as temperature and emotional status on hyperhidrosis, an accurate evaluation about the effect of BTX-A on axillary hyperhidrosis may be rather difficult.

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Dermatomyositis without muscle weakness associated with transitional cell carcinoma of the bladder

To the Editor

A 63-year-old man presented with a 1-month history of skin eruptions on his face, chest and the extensor aspects of his elbows, hands and knees. He had no history of muscle weakness. Physical examination revealed heliotrope erythema, oedema of the upper eyelids, diffuse erythema and telangiectasia on his face and 'V' of the chest (fig. 1); there was violaceus erythema on the proximal interphalangeal joints, elbows and knees (Gottron's sign). The man presented no clinically detectable muscle weakness by manual strength test.

Laboratory investigations revealed normal complete blood count and biochemistry profile. Anti-streptolysin-O, C-reactive protein, rheumatoid factor, antinuclear antibody and anti-double-strand DNA were negative. Erythrocyte sedimentation rate was 24 mm/h. Creatine phosphokinase (CPK) level was

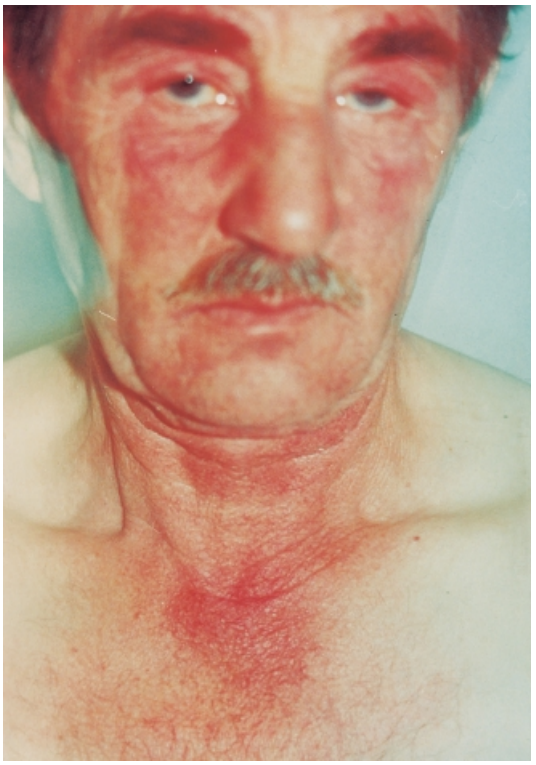

fig. 1 Erythema and oedema of the upper eyelids, diffuse erythema on the face and 'V' of the chest.

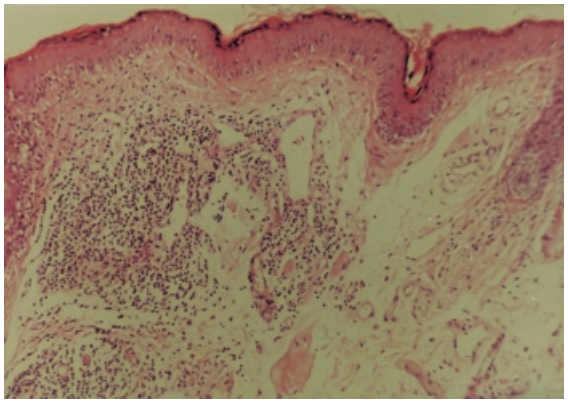

fig. 2 Histological picture of a skin specimen showing thinning of the epidermis, enlargement of blood vessels, and perivascular infiltrate of lymphocytes (haematoxylin and eosin, original magnification × 100).

44 U/L (normal 24–195) and aldolase 5 U/L (normal 3.1–7.6). A biopsy specimen was obtained from the lesion on the face. The findings of the histopathological examination were consistent with dermatomyositis (DM), showing thinning of the epidermis, hyperkeratosis, hydropic degeneration of the basal cell layer, and perivascular lymphocytic infiltrate in the dermis. There was homogeneous eosinophilic fibrinoid deposition along the dermoepidermal junction (fig. 2). Histopathological examination of the specimen obtained from the deltoid muscle was consistent with inflammatory myositis, but the findings of electromyography (EMG) and the serum levels of CPK and aldolase were normal.

Based on these clinical and laboratory findings the case was diagnosed as DM without muscle weakness, and systemic corticosteroid therapy (1 mg/kg daily) was initiated. Two months after beginning therapy, the man began to experience abdominal pain and fever. Haematuria and pyuria were detected. Abdominal ultrasound revealed hydronephrosis, in particular in the left kidney, and intravenous pyelography and cystoscopy evidenced a mass in the bladder. This mass was identified histopathologically as transitional cell carcinoma and was treated by surgery. The skin lesions revealed slight improvement with systemic corticosteroid therapy, but this treatment was tapered gradually before the surgery. The diagnosis was confirmed as DM without muscle weakness since no clinical or laboratory findings characteristic of myositis were detected throughout the follow-up period for 3 years; the man was prescribed sunscreens to protect the skin lesions during the follow-up period.

DM is characterized by cutaneous findings and inflammatory myositis. Characteristic cutaneous lesions of DM include a violaceous or heliotrope periorbital eruption or oedema, periungual telangiectasia, poikiloderma, photosensitivity, Gottron's papules and Gottron's sign. Cutaneous lesions may often precede clinical myositis and muscle weakness develops 3–6 months later in most patients. However, in some patients, muscle disease does not develop or appears to be minor or transient.[1–3] Therefore, the term 'amyopathic DM' (ADM), as described by Euwer and Sontheimer, is used to refer to patients who have classical cutaneous findings without clinical or enzymatic evidence of muscle disease for at least 2 years.[1] Cosnes *et al*.[2] designated their cases as DM without muscle weakness. However, controversy still exists concerning the definition of muscle disease. Those subjects who do not have overt muscle weakness or abnormal laboratory parameters are sometimes considered to be ADM.[1–3] On the contrary, some authors believe that the presence of minimal muscle involvement is inconsistent with the diagnosis of ADM.[4,5] Moreover, there is debate about the necessity of further investigations, such as EMG and in particular muscle biopsy, in cases where there is no overt muscle weakness. These diagnostic investigations are aggressive, and some authors emphasize that EMG and muscle biopsy are less sensitive than muscle enzyme studies for the detection of muscle disease.[1,6] We diagnosed our case as DM without muscle weakness because the man had no clinical and laboratory findings regarding muscle involvement except for the muscle biopsy.

There is still no consensus about the treatment of ADM. Some authors administer systemic corticosteroids to prevent the development of muscle weakness;[1] others avoid systemic corticosteroids, suggesting that ADM should be treated with antimalarial therapy instead because the adverse effects of corticosteroids must be balanced against the benign course of the disease and the rash of DM can be refractory to systemic corticosteroid therapy.[2,3] We prescribed corticosteroid therapy to prevent the development of muscle weakness, but we stopped the treatment 2 months later because of the onset of bladder carcinoma. We did not detect muscle weakness during the therapy, and the man's skin lesions did not improve markedly; moreover, the skin lesions persisted after the treatment of the cancer.

There have been reports of cases of ADM associated with an underlying malignancy, including lymphoma,[7] carcinoma of the lung, ovary, uterus,[8] breast,[2,6,7] colon,[4] kidney[7] and nasopharynx.[9] Bladder carcinoma is less frequently encountered in association with DM,[10] and to the best of our knowledge, the association of DM without muscle weakness, and transitional cell carcinoma of the bladder has not been reported previously.

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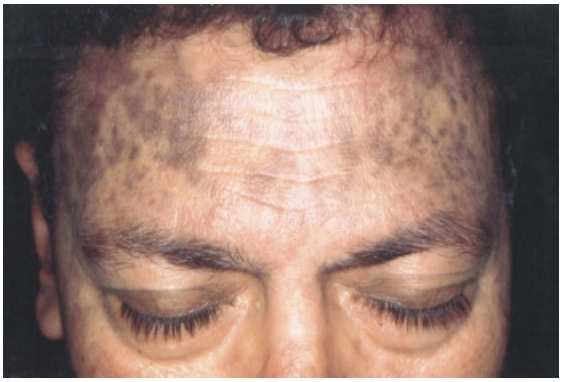

fig. 1 Brown violaceous annular plaques on the forehead.

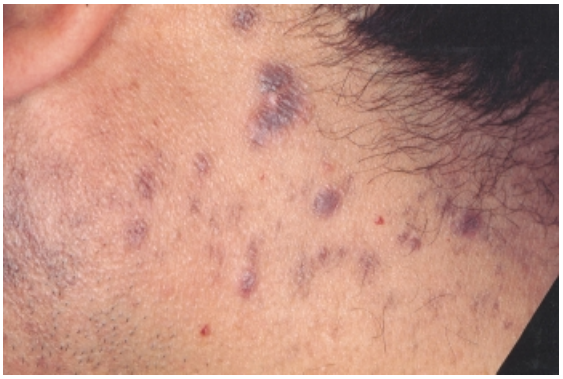

fig. 2 Lichenoid papules on the neck.

Lichen planus actinicus treated with acitretin and topical corticosteroids

To the Editor

Lichen planus actinicus, which is also known as lichen planus tropicus,[1] lichen planus subtropicus,[2] lichenoid melanodermatitis,[3] and lichen planus atrophicus annularis,[4] is a distinct variant of lichen planus, affecting mainly children and young adults. The majority of reported cases are from the Middle East, but cases from the Netherlands,[5] Italy,[6] Tunisia,[7] India,[8] East Africa,[3] the United States[4,9] and other countries have also been described. Clinically, four types of lichen planus actinicus can be distinguished: annular, plaque-like, dyschromic, and pigmented. The most common form is the annular type, which consists of erythematous brownish plaques with an annular configuration. In the plaque-like type, the lesions have a depressed brownish centre and an erythematous elevated border, sometimes resembling granuloma annulare. The dyschromic type presents as discrete and confluent whitish angular papules. Finally, the pigmented type consists of hypermelanotic patches, sometimes assuming a melasma-like appearance.[6,10]

A 51-year-old Tunisian patient presented with a 2-year history of asymptomatic skin lesions on his face, neck, and hands. The dermatosis started in summer and improved markedly during winter, but relapsed during the next sunny season. There was no prior injury or inflammation in these areas. The patient had no history of any contact with or intake of any drugs either.

Clinical examination revealed numerous brown violaceous annular plaques located on the forehead (fig. 1), lateral parts of the neck (fig. 2), and dorsal aspect of the hands. These lesions had a tendency to coalesce, forming circinate plaques. Some lichenoid papules on the neck could also be observed (fig. 2). The remaining parts of the skin and the mucous membranes were normal, and the nails were not affected.

A biopsy specimen was obtained from a representative lesion on the forehead. Microscopic examination revealed epidermal parakeratosis and coarse vacuolar degeneration of the basal cell layer. Dyskeratotic cells were noted. A band-like predominantly lymphocytic infiltrate with a few histiocytes in the papillary dermis was present. There was also marked pigmentary incontinence. Pigment was found in macrophages and as large extracellular clumps.

Immunofluorescence studies showed deposits of IgM and fibrin on necrotic keratinocytes. Routine laboratory investiga-

tions yielded normal values for the total blood cell counts, erythrocyte sedimentation rate, hepatic and kidney function tests, serum protein and electrolyte levels, antinuclear antibody test, and urinalysis.

The patient was treated with acitretin, 0.5 mg/kg body weight per day for 4 months, and 0.1% betamethasone dipropionate cream, once a day for 2 weeks. Protective measures against natural ultraviolet (UV) irradiation were taken, and he was also instructed to avoid sun exposure as much as possible. Clearing of lesions began in the first 2 weeks and complete resolution occurred after 2 months of therapy. The eruption did not recur in the following summer.

The cause of lichen planus actinicus is unknown; however, UV irradiation appears to be the major precipitating factor. The lesions develop mainly in sun-exposed areas, with particular predilection for the face. However, covered parts of the skin and buccal mucosa can sometimes be involved.[2,11] Nails and covered parts of the scalp are spared. Pruritus is minimal or absent. There is no Koebner phenomenon. The eruption usually appears during the spring and summer, and improvement or even complete remission takes place during the winter, leaving hyperpigmented patches. However, relapse or aggravation may occur during subsequent sunny seasons. As lichen planus actinicus has a racial predilection affecting predominantly individuals of oriental origin, it is likely that a combination of environmental factors and genetic predisposition may be important in the pathogenesis of the disease.

Induction of lesions by artificial light sources has been attempted. With the use of a Kromayer lamp for repeated exposure on five successive days, Katzenellenbogen[12] succeeded in provoking lesions in two of 11 patients tested. Likewise, Isaacson *et al.*[9] used repeated UVB irradiations, each six times the minimal erythema dose, from a xenon-arc solar simulator and were able to induce discrete lichenoid papules that faded in 7 days. Van der Schroeff *et al.*,[5] using repeated doses of UVB irradiation, successfully induced lichenoid lesions on the lower portion of the back of a patient who had involvement of the exposed parts of the skin and buccal mucosa.

Several modalities for treating lichen planus actinicus have been tried, including Grenz rays,[4,12] bismuth,[1] arsenic compounds,[11] and topical corticosteroids, with or without occlusion, but with inconclusive results. Antimalarial agents[13] and intralesional corticosteroids combined with topical sunscreens[2] have been reported to be successful in some cases. In our patient, a therapeutic regimen, including acitretin and topical corticosteroids along with sun protection measures, led to complete resolution of all skin lesions within 2 months. Although the aromatic retinoid acitretin has proved to be successful in the treatment of lichen planus in its classic form because of its keratolytic and anti-inflammatory activities, its role in lichen planus actinicus has not been investigated so far.

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Perioral dermatitis successfully treated with topical adapalene

To the Editor

Perioral (rosacea-like) dermatitis is a well-known entity, characterized by facial eruption of papules, papulopustules, and papulovesicles on an erythematous and scaling base around the mouth, and a burning sensation.[1] Periorbital[2] and perinasal lesions may also occur. In patients with the granulomatous (lupoid) variant, discrete flesh-coloured papules are a prominent feature.[3] Perioral dermatitis occurs predominantly in adult women, although it has also been reported in men and

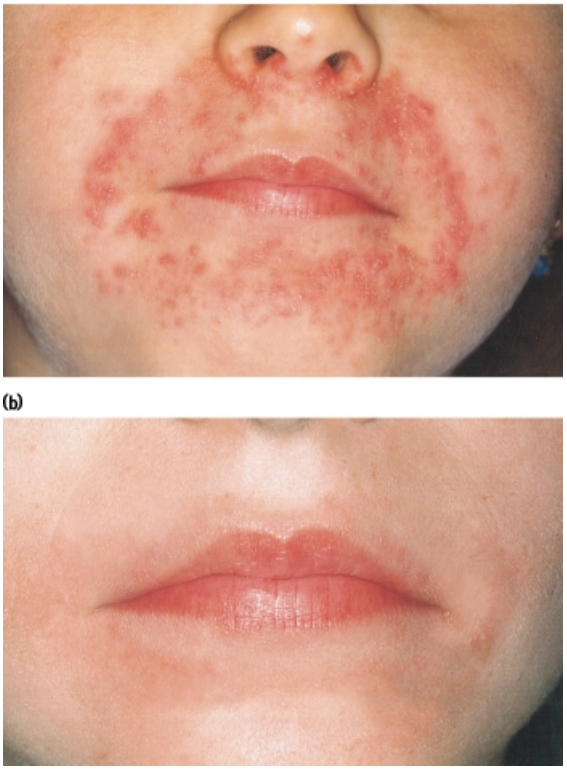

fig. 1 Multiple discrete papules, papulopustules, and papulovesicles around the mouth before (a) and after (b) treatment with topical adapalene.

children.[3] The pathogenesis of the condition is unknown, but it is related to impairment of barrier function and dryness of the skin as well as proliferation of the skin flora. It may be induced by topical application[4] or inhalation[5] of corticosteroids, allergic response to amalgam and mercury in dental fillings,[6] toothpaste containing fluorides,[7] cosmetics,[8] rosin in chewing gum,[9] fusiform bacteria,[10] *Candida albicans*,[11] and *Demodex folliculorum*.[12] Many authors consider the treatment of perioral dermatitis to be a frustrating experience. However, there have been several reports of beneficial effects from oral tetracycline, oral erythromycin, oral isotretinoin (13-*cis*-retinoic acid), and various local measures, including erythromycin and metronidazole, in the treatment of this condition. A case of perioral dermatitis is presented that responded promptly and with no side-effects to the topical application of adapalene 0.1% gel.

A 32-year-old white woman presented with an unremarkable medical history and no previous skin eruptions. Skin lesions had suddenly appeared around her mouth. She had only slight itching. No history of an obvious contactant was elicited. Corticosteroids were not used. She was given a 2-week course of 2% erythromycin solution without improvement.

Clinical examination 5 weeks after onset of the skin eruption revealed multiple minute skin-coloured papules, papulopustules, and papulovesicles, located around the mouth (fig. 1a). The lesions became confluent in some areas. A small degree of scale was present. There was a zone of sparing immediately adjacent to the lips.

A skin biopsy specimen taken from the perioral area revealed a superficial and deep perivascular lymphohistiocytic infiltrate, centred around hair follicles, beneath an acanthotic epidermis, with mild hyperkeratosis. Granulomas could not be observed. Special stains for fungi were negative.

Bacterial and fungal cultures from facial skin as well as patch tests with standard substances were negative. Stool sampling for the presence of *Candida albicans*, which was performed on three different occasions, revealed a non-significant gastrointestinal colonization with *Candida albicans* ($< 10^3$ c.f.u./g stool).

The eruption disappeared after 4 weeks of topical treatment with adapalene 0.1% gel without systemic medication (fig. 1b). The agent was applied once a day at night without any side-effects. We recommended the patient to discontinue the use of cosmetics and moisturizers until all skin lesions had resolved. No recurrence was seen during an 8-month follow-up period after discontinuing treatment.

Adapalene is a synthetic naphthoic acid derivative with retinoid-like activity, but a distinctly different chemical structure.[13] It is a potent modulator of cellular differentiation, keratinization, and inflammatory processes, whose mechanism of action is believed to be similar to that of other retinoids. Adapalene interacts with nuclear retinoic acid receptors and is selective for the RAR-β and RAR-γ receptors, while it does not interact with RXR receptors. It has been hypothesized that this receptor selectivity may cause adapalene to have a greater effect on keratinocyte differentiation than proliferation. In a number of *in vitro* and *in vivo* animal models, it has been shown to possess moderate to potent anti-inflammatory activity compared with corticosteroids, such as betamethasone and non-steroidal anti-inflammatory drugs.[14] In the same models, tretinoin and isotretinoin were found to have either weak or no anti-inflammatory activity. Part of this anti-inflammatory activity may be related to its ability to interfere with polymorphonuclear leucocyte functions and arachidonic acid metabolism. It is likely that the efficacy of adapalene in perioral dermatitis is due to its anti-inflammatory activity.

It appears preferable to use an effective and well tolerated topical regimen instead of a systemic regimen to avoid unwanted side-effects. Adapalene has been used with success in the management of mild to moderate acne vulgaris.[14] This report provides evidence of its efficacy in the treatment of perioral dermatitis. Adapalene 0.1% gel has been shown to have a low skin irritation potential even when applied immediately after washing.[15] Freedom from complicated treatment regimens may result in better patient compliance and greater treatment success. Further clinical trials are necessary to confirm these preliminary results.

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Poor prognosis of acute myeloid leukaemia associated with leukaemia cutis

To the Editor

Leukaemia cutis is characterized by skin infiltration of malignant haematopoietic cells and usually occurs with bone marrow, peripheral blood, and internal organ involvement. It is seen in adult patients and manifests with multiple localized or generalized papules, plaques or nodules with a characteristic reddish or violaceous colour in the context of known leukaemia, e.g. acute myeloid leukaemia (AML) or chronic myeloid leukaemia (CML). However, some reports describe the appearance of skin involvement in the absence of other signs of leukaemia. Specific cutaneous involvement has been reported in 10–50% of patients with AML of the French–American–British (FAB) classification subtypes M4 and M5, up to 10% of patients with AML–FAB subtypes M0, M1, M2 and M3, and in about 2% of patients with CML.[1,2] Dreizen *et al*.[3] reported that mucous lesions of leukaemia, e.g. gingival hyperplasia, occurred in 3.6% and leukaemia cutis in 3.1% of 1.076 patients with leukaemia. However, only 7.6% of those with leukaemic infiltrates had simultaneous gingival and skin involvement. We describe a patient with AML associated with mucocutaneous lesions.

A 43-year-old woman presented with a 6-week history of skin lesions that gradually spread out on the face, trunk, and extremities. She had had malaise and intermittent fever for a few days. Physical examination showed submandibular and cervical lymphadenopathy as well as hepatomegaly. Widespread reddish papules and plaques were present, especially on the face and trunk. Gingival hyperplasia and purpuric papular lesions on the extremities could also be observed. Pathological laboratory findings were as follows: erythrocyte sedimentation rate 54 mm/h, haemoglobin 10 g/dL, haematocrit 31.8%, white blood cell count 7600/μL and thrombocytes 15 000/μL. Repeated haemocultures were negative. A skin biopsy was taken from the back. The microscopic examination revealed an interstitial leukaemic infiltrate. The so-called reticular pattern of infiltration was marked by diffuse permeation of the dermis by leukaemic cells in strands between collagen bundles. The myelomonocytic cells had large atypical nuclei with scant cytoplasm. Bone marrow examination confirmed a diagnosis of AML, type M5 according to the FAB classification.[1] Immunophenotyping of leukaemic cells in the peripheral blood revealed 35% myeloblasts, which were positive for CD33 and CD45. Chromosomal analysis (standard Giemsa banding technique) was performed in 12 metaphases. Addition 6p+ and deletion 11q– was found in six karyotypes. The patient was treated with cytarabine, idarubicine, and cyclophosphamide, respectively. As the disease could not be controlled by chemotherapy, a bone marrow transplantation was performed. Nevertheless, the patient died 12 months later with disseminated disease.

Non-specific lesions (leukaemids) are common, occurring in approximately 30% of patients with leukaemia. Leukaemids may be related to anaemia, thrombocytopenia, infection or drugs, or result from immunological responses to tumour antigens.[4] In general, specific lesions show a diffuse infiltration of leukaemic cells into the dermis and subcutis. Extensive involvement and disruption of blood vessels and skin adnexa are

characteristic features in granulocytic, monocytic, and myelomonocytic leukaemia cutis. However, biopsy specimens of skin from patients with different types of leukaemia show a wide range of histopathological changes that are variable among the different types of leukaemia and sometimes even among different patients with the same type of leukaemia. Moreover, differentiation of specific cutaneous infiltrates from lymphoproliferative and inflammatory skin conditions may be challenging. In most cases, immunohistochemical study is necessary to characterize immunophenotypes of tumour cells. Negativity of pan-T and pan-B markers (CD3 and CD20) and positivity of granulocyte markers are key diagnostic features. Specific gene abnormalities related to chromosome translocations are considered to be closely associated with the pathogenesis and clinical characteristics of leukaemias. The t(10;11) abnormality involving the short arm of chromosome 10 and the long arm of chromosome 11 has previously been reported in acute leukaemias.[5,6]

Accurate identification is important in scheduling adequate management of patients with leukaemia, in particular in cases where skin lesions are the first clinical sign of the disease. Nevertheless, leukaemia cutis is considered to be a poor prognostic sign in patients with systemic leukaemia – despite aggressive therapies, most patients die within a few months. Conventional chemotherapy regimens are advocated in leukaemia cutis. Small skin lesions may be successfully treated with surgical removal or local radiotherapy. Whole body electron-beam radiation therapy is considered to be beneficial in widespread skin involvement.[7] The presented case of AML associated with leukaemia cutis exemplifies the fatal prognostic meaning of this association.

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Azelaic acid (20%) cream in the treatment of acne vulgaris

To the Editor

Azelaic acid (AZA) is a naturally occurring saturated nine-carbon dicarboxylic acid (COOH-$(CH_2)_7$-COOH), possessing a variety of biological actions both *in vitro* and *in vivo*.[1] AZA has insignificant effects on normal cells.

The physiopathological mechanism of acne seems to depend on several factors: (i) a hyperkeratinizing process of follicular channels; (ii) microbial colonization of pilosebaceous units; (iii) perifollicular inflammation; (iv) sebum production and excretion; and (v) differential rates of conversion of testosterone to dihydrotestosterone.[1]

AZA is an antikeratinizing agent displaying an antiproliferative cytostatic effect on keratinocytes (by inhibiting DNA synthesis) and modulating the early and terminal phases of epidermal differentiation (by inhibiting cytoplasmic protein synthesis).[2] Both *in vitro* and *in vivo*, AZA cream has an antibacterial effect,[3,4] which is primarily initiated by the inhibition of the bacterial protein synthesis.[5] The application of 20% AZA cream over a 3–6-month period did not affect excretion rate[6,7] or composition of sebum[2] or the morphology of sebaceous glands[2] in acne patients. Nevertheless, patients with acne using AZA for 1–2 months, reported subjectively gradual and progressive reduction in skin greasiness.[3] AZA's effect on testosterone metabolism remains controversial. AZA also has an antipigment effect, probably through its competitive inhibition of oxido-reductive enzymes, such as tyrosinase, and mitochondrial respiratory enzymes.[1]

Topical 20% AZA cream applied twice daily for 6 months was of comparable efficacy with topical 0.05% tretinoin cream,[8] topical 5% benzoyl peroxide gel,[7] topical 2% erythromycin cream[9] and oral tetracycline 0.5–1.0 g/d in comedonal and mild–moderate (80%) and moderate–severe (60%) inflammatory types of acne.[4,10]

We conducted an open prospective study, including 46 patients (19 men and 27 women), aged 14–25 years, with recurrence of acne or inadequate acne response to other therapies. The study ran from the month of February until April of the following year. Acne grading was based on the Cunliffe score (Leeds technique), a photonumeric grading scale.[6] Inclusion criteria for this study were patients over 14 years of age, with acne grades 1–3 (without cystic acne). All previous acne treatments (comedolytic preparations, local antibiotics and oral

Table 1 Grading of acne vulgaris in patients at each visit

Acne vulgaris	Week 0	Week 3	Week 9	Week 15	Week 24	Week 30
Grade 0–1	0	1	7	21	36	34
Grade 1–2	31	31	27	14	1	3
Grade 3	9	8	6	5	3	3

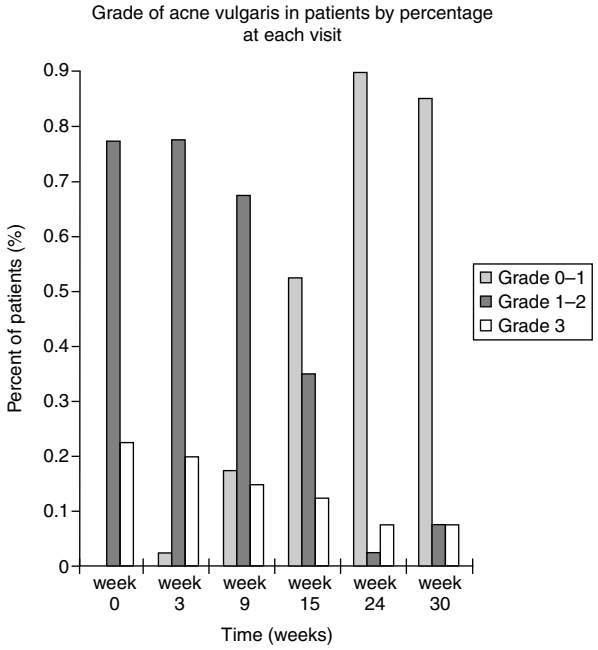

fig. 1 Grade of acne vulgaris in patients by percentage at each visit.

minocycline) were discontinued 1–3 months, respectively, prior to this study. Patients applied topical 20% AZA cream (Skinoren®, Schering Berlin, Germany) on affected areas once a day for the first week and twice a day for the next 23 weeks. All patients were told the cream may cause mild stinging and to apply a very thin layer. Follow-up visits were required at the beginning of the study, and then at weeks 3, 9, 15, 24 (end of treatment) and 30 (6 weeks after end of treatment). All patients were examined by the same investigator before the study and throughout the study period.

Forty patients (87%) completed the study. Drop-outs were those who failed to attend a follow-up session, not due to side-effects. Before treatment, no patients (0%) had 0–1 grade acne vulgaris, 31 patients (77.5%) had grade 1–2 acne and nine patients (22.5%) had grade 3 acne. At week 30, 34 patients (90%) were in grade 0–1 acne and were satisfied from the decrease in comedone number and in the number of papular and pustular lesions (see Table 1 and fig. 1). At week 30, hyperpigmentation in resolving acne in our 26 patients with Fitzpatrick skin complexion of 3–4 was assessed. Of those 26 patients, at the beginning of the study, 23 (88%) had grade 1–2 acne vulgaris and three (12%) had grade 3 acne. At week 30, 22 patients (85%) had grade 1–2 or 0–1 acne, with mild or no hyperpigmentation where lesions had resolved. In resolved lesions, the skin was the same pigmentation as uninvolved skin. Four patients (15%) remained with hyperpigmentation and acne grade 1–3. No serious adverse effects were noted. There were three cases of mild stinging sensation that resolved spontaneously and did not require stopping the trial.

Although effects on pigmentation were not assessed at the beginning of treatment and at each follow-up session, AZA may be an ideal choice in treatment in patients with acne, especially those with a tendency for hyperpigmentation, and should be considered in the rare case of a patient with both acne and melasma occurring simultaneously. We recommend a large controlled study with follow-up visits at 3–4-week intervals, to investigate these findings further.

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Neurofibromatosis type I and Arnold–Chiari malformation

To the Editor

Neurofibromatosis type I (NFI) is the most common neurocutaneous syndrome characterized by a large variety of clinical features. Cerebral dysplasias are also associated with NFI. Arnold–Chiari type I malformation was first reported by Chiari in 1891 as an 'abnormality of posterior cranial fossa',[1] unknown by aetiology. It is described as a dysplasia of the nervous system, consisting of herniating cerebellar tonsils into the magno foramen. During neuroradiological screening this malformation is occasionally found as an asymptomatic syndrome in patients affected by NFI; initially, this association was being described as accidental.[2,3] At the moment only 10 cases of this syndrome associated with NFI have been reported in the literature.[4,5] We report two cases of NFI associated with the Arnold–Chiari malformation.

The first case came to our observation showing axillary freckles, café-au-lait spots, spreading all over the body, and cutaneous and subcutaneous diffuse neurofibromas. On the plantar region of the left foot an oval plexiform neurofibroma (6 cm in diameter) was present. A plexiform neurofibroma was found on the left arm too. On the basis of these data, according to criteria from the NIH Consensus Conference,[6] we made a diagnosis of NFI. The patient did not present a family history of NFI and the ophthalmological exam revealed the presence of iris Lisch nodules. The patient underwent magnetic resonance (MR) of the brain and medulla, which showed an Arnold–Chiari type I malformation, with cerebellar tonsils herniated into the foramen magno and an elongation of the fourth ventricle.

The second patient, affected by NFI, presented café-au-lait spots, spread on the trunk, axillary and inguinal freckles and subcutaneous neurofibromas. The patient was below average height and weight and mentally retarded. His mother and brothers were also suffering from NFI. Neurological exam showed: (i) an ataxic and spastic gait; (ii) dysmetria of the upper limbs; (iii) Hoffman's reflex and Babinski's sign were bilaterally positive; (iv) and nystagmus was present. The electroencephalogram was negative and computed tomography of the brain demonstrated a marked hydrocephalus of the three ventricules. MR of the brain and the spinal marrow confirmed a swelling of the ventricular supratentorial system, with stenosis of the mesencephalic aqueduct with cerebellar tonsils herniated into the foramen magnum. A diagnosis of Arnold–Chiari malformation type I was made.

NFI is a multisystemic disease with an autosomal dominant transmission, characterized by café-au-lait spots, cutaneous neurofibroma, skeletal, vascular abnormalities and neurological diseases.[3,6] In patients with NFI, typical lesions of the central nervous system (CNS) include: macrocephaly, unilateral sphenoidal dysplasia, glioma of the optic chiasma, meningiomas and schwannomas of cranial nerves and unidentified bright objects, located at the cerebellum, basal ganglions, thalamus and base of the brain.[2,3] Patients suffering from NFI can develop hamartomas of the CNS, heterotopic damage, stenosis of the mesencephalic aqueduct and vascular malformations.[2,7,8]

Rarely, Arnold–Chiari malformation is associated with NFI. According to severity, Arnold–Chiari malformation can be classified into three types: (i) type I, characterized by herniating of the brain tonsils into the high brain medullary arachnoid spaces; (ii) type II malformation, with dislocation of the fourth ventricle vs. the base of the bulb, and dislocation of the part of the cerebellum into the brain duct; and (iii) type III malformation secondary to brain schism with cerebellum encephalocele.[9] Patients with type I are asymptomatic in the majority of cases,[4] while some subjects can present signs and symptoms of cerebellum compression such as ataxia, nystagmus, gait difficulties, opisthotonos, Horner's syndrome and paralysis of the last cranium nerves. Children prematurely damaged by Chiari's syndrome in utero may present at birth with apnoea crisis, scratching, dysphonia, persistent crying, syncope, dysphagia, incontinence and can die suddenly shortly after birth. Arnold–Chiari malformation can include the presence of alterations of the CNS such as stenosis of the Silvio aqueduct, the syringomyelia and meningomyelocele.[10] The headache situated in the occipital region is one of the typical signs in adults suffering from Chiari's disease and it augments with Valsalva movements, while in children there is a high incidence of scoliosis and it is considered as a negative prognostic factor.[5]

This association of NFI and Arnold–Chiari malformation could be considered a coincidence. However, on the basis of the literature data, the frequent observation in subjects with NFI, of lesions affecting the nervous system such as bifid spine, hydrocephalus, meningocele and of bony lesions, such as scoliosis, macrocephalia and dysplasia of the sphenoid, could confirm the hypothesis of an osteogenetic and neural abnormal development common to both diseases, which suggests a congenital neuroaxial dysgenesia as a possible common pathogenic mechanism.

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Treatment with pentoxifylline in Behçet's disease

To the Editor

Behçet's disease is a complex multisystem disease with considerable clinical diversity. Neutrophil motility and superoxide production are characteristically increased in patients with Behçet's disease. Pentoxifylline modulates membrane receptor-mediated functions,[1] neutrophil motility[1,2] and superoxide anion production.[2,3] Successful treatment of Behçet's disease with pentoxifylline was recently reported.[4] We observed two subjects with Behçet's disease who showed beneficial effects to treatment with this drug.

Case 1 is a 17-year-old female with recurrent oral and vulvar (fig. 1) ulceration, uveitis and pseudofolliculitis and had experienced 5 months of persistent painful vulval ulceration, amaurosis, fever, and knee and wrist arthralgia, in spite of continuous treatment with prednisone (30–60 mg/d) and azathioprine (150 mg/d); colchicine had previously been unable to control the disease. Laboratory tests showed normal findings except for elevated C-reactive protein (CRP–12.3). Fluorescein angiography showed retinal vasculitis on the left eye. Prednisone and azathioprine were maintained at the same dose and oral pentoxifylline was introduced at a dosage of 400 mg twice a day. After a week of treatment we observed complete remission of the vulvar lesions, normalization of CRP levels and improvement in the retinal vasculitis. The prednisone dose was slowly reduced to 10 mg/d and azathioprine to 100 mg/d, but the pentoxifylline dosage was maintained. After 4 months the patient remains without clinical or laboratory signs of disease activity.

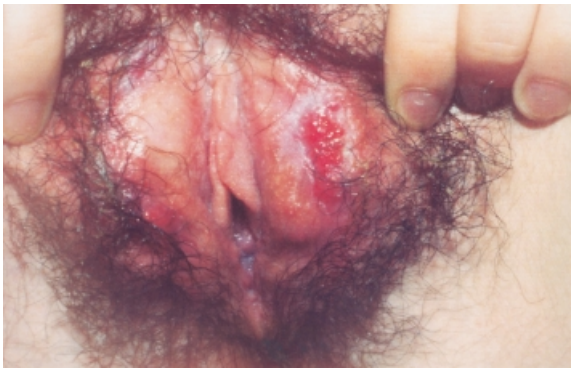

fig. 1

Case 2 is a 32-year-old female with vulvar and oral ulceration, bilateral uveitis, erythema nodosum and arthralgia; she was administered prednisone (60 mg/d) and azathioprine (150 mg/d) without improvement. Laboratory findings were normal except for CRP (9.0). Fluorescein angiography showed bilateral retinal vasculitis. Both drugs were maintained in the same dose and pentoxifylline was introduced at a dosage of 400 mg twice a day.

After 10 days of treatment with pentoxifylline we observed complete remission of lesions, with normalization of CRP and improvement in the retinal vasculitis. The dosage of prednisone was reduced to 15 mg/d and azathioprine to 100 mg/d, but the pentoxifylline dosage was maintained at 400 mg twice a day. After 5 months the patient remains without clinical signs of disease activity.

Yasui *et al.*[4] reported improvement of ocular symptoms in three males with Behçet's disease after 2 weeks of treatment with pentoxifylline. Neutrophil motility returned to normal in all three men.

In our two subjects colchicine, steroids and azathioprine had not been effective. Cyclosporin and cyclophosphamide account for important side-effects and thalidomide was contraindicated due to its teratogenous potential. The vulvar ulceration and

retinal vasculitis improved in both women after 1 week of therapy with pentoxifylline.

As reported in our cases non-effective therapy (prednisone and azathioprine) was maintained, and the beneficial effects may be due to the pentoxifylline itself or to synergy. It is important to observe that remission was maintained in spite of steroid and immune suppressor dose reduction. Our cases support previous studies of the efficacy of pentoxifylline in ocular disease[4] and, in our opinion, also in vulvar disease. A randomized controlled study should be done for a definitive statement on this matter.

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Toxic epidermal necrolysis due to cotrimoxazole

To the Editor

Toxic epidermal necrolysis (TEN) is a life-threatening, rapidly evolving mucocutaneous reaction characterized by widespread erythema, necrosis and bullous detachment of the epidermis resembling the effects of scalding, constitutional symptoms and internal organ involvement. The mortality rate is high and sequelae due to mucosal scarring are frequent and often severe. TEN usually represents a drug-induced, dose-independent hypersensitive reaction, but may result from a variety of infections, or have no clear cause.[1] The most common offending agents are sulphonamide antibiotics (especially the trimethoprim–sulphamethoxazole combination), anticonvulsants (barbiturates and carbamazepine) and allopurinol.[2,3] The condition is most commonly associated with ocular complications and sepsis, gastrointestinal haemorrhage, and fluid and electrolyte imbalance leading to renal insufficiency.[1,4] Treatment of TEN is usually based on removal of the offending drug, fluid replacement, nutritional support and local management.[5] Broad-spectrum antibiotics, such as erythromycin, which have little potential for sensitization, should be chosen.[2,6] Skin care should be aimed at rapid healing and prevention of infection. Glucocorticoid therapy is still under discussion.[2] High-dose corticosteroid therapy has been the most commonly advocated treatment, but, more recently, this has changed to a non-steroid protocol.[7,8] Whereas the parenteral use of glucocorticoids has been found useful in the early phase of drug-induced TEN, in some cases it has been considered not to provide any benefit and to mask signs of impending sepsis, increase risk of infection and impair wound healing.[1]

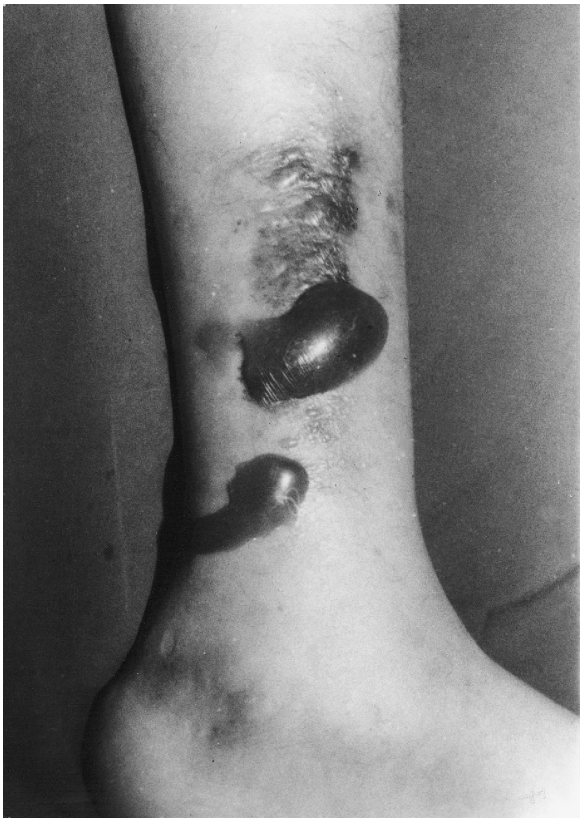

fig. 1

We report the case of an 86-year-old male patient who developed a severe and extensive clinical feature of TEN within 24 h after cotrimoxazole (trimethoprim–sulphamethoxazole) administration due to urinary infection. Anamnestic data revealed noted allergic reaction to cotrimoxazole a few years before. On admission the patient was acutely ill with widespread erythematous exanthem affecting most of his skin. There were multiple flaccid blisters and erosions on the upper trunk, and Nikolsky's phenomenon was positive. According to the role of Wallace '9', 35% of the skin surface was affected with denuded areas and bullae (fig. 1). The oral and genital mucous membranes showed inflammatory reddening with diffuse erosions. The conjunctivae were inflamed with mucoid drainage.

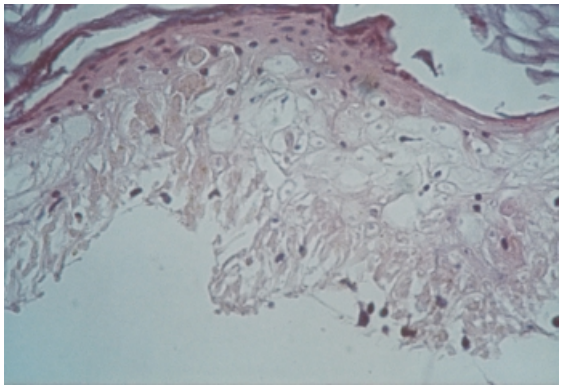

fig. 2

The man was disorientated, confused and somnolent with high fever, dyspnoea and lassitude. He presented signs of dehydration: he was oliguric and hypotensive, skin turgor was decreased and the oral mucous membranes were dry. In the course of hospitalization the man developed a psychotic reaction with notable psychomotor agitation.

Histopathological examination revealed typical findings for TEN with full-thickness epidermal necrosis and detachment from the dermis partly with subepidermal blistering. The upper dermis revealed a dense perivascular infiltrate of lymphocytes and histiocytes (fig. 2). Because of the great risk of infection and the tendency for losing large amounts of body fluids from the extensive areas of eroded skin, the man was treated in an intensive care burn unit according to the rules for severe burns, with removal of the offending drug, fluid replacement, antibiotics, nutritional support and topical measures. On admission we had administered medium doses of corticosteroids and parenteral antihistamines for the first 2 days and an antibiotic was administered due to urinary infection. Constant ophthalmological care prevented ocular complications. Local treatment included regular care of denuded areas with epithelization promoting creams as well as vaseline and bio-occlusive dressings. The man showed excellent recovery after 1 month of intensive, interdisciplinary care by an internist, a dermatologist, a surgeon, a psychiatrist and an oculist. The skin lesions healed completely with some poikilodermic and atrophic sequelae.

Our patient developed acute disseminated epidermal necrosis with exfoliation of large areas of the skin. Anamnestic data revealed noted allergic reaction to cotrimoxazole. As the lesions manifested very soon after drug intake we consider the drug to be causally implicated. Cotrimoxazole is an antimicrobial drug belonging to the sulphonamide group that is commonly cited as the cause of TEN.[1,6] Histopathological examination revealed typical findings for TEN with full-thickness epidermal necrosis and subepidermal split. Despite his very serious conditions our patient responded well to the treatment and did not develop complications.

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Lichen sclerosus et atrophicus of the scalp: satisfactory response to acitretin

To the Editor

Lichen sclerosus et atrophicus (LSA) is a rare, chronic, inflammatory disease that can affect any skin site, commonly localized in the genital area. Extragenital involvement has been reported involving the upper trunk, neck, wrists, thighs, face and forehead.[1–3] Uncommon presentations include lesions on the oral mucosa[4] and scalp.[5–8] Although extragenital lesions have not been reported to be associated with malignant change, treatment is necessary to relieve symptoms and progression of the disease and to prevent further scarring.[1] Topical corticosteroids,[2] testosterone propionate[1] and systemic retinoids[9] have been administered with variable success. We present the case of a male patient with an unusual scalp localization of LSA and a good response to acitretin treatment.

A 57-year-old man who had been suffering from itchy lesions on the scalp for 2 years was unsuccessfully treated with topically applied steroids. His previous medical history was normal except for excessive sun exposure. He noted no familial occurrence. Clinical examination revealed well-defined, violaceous brownish plaques of different sizes with a slightly atrophic centre on the frontal and parietal regions of the scalp (fig. 1)

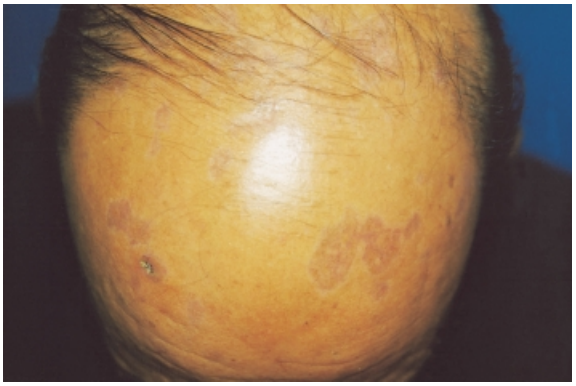

fig. 1 Lichen sclerosus et atrophicus of the scalp.

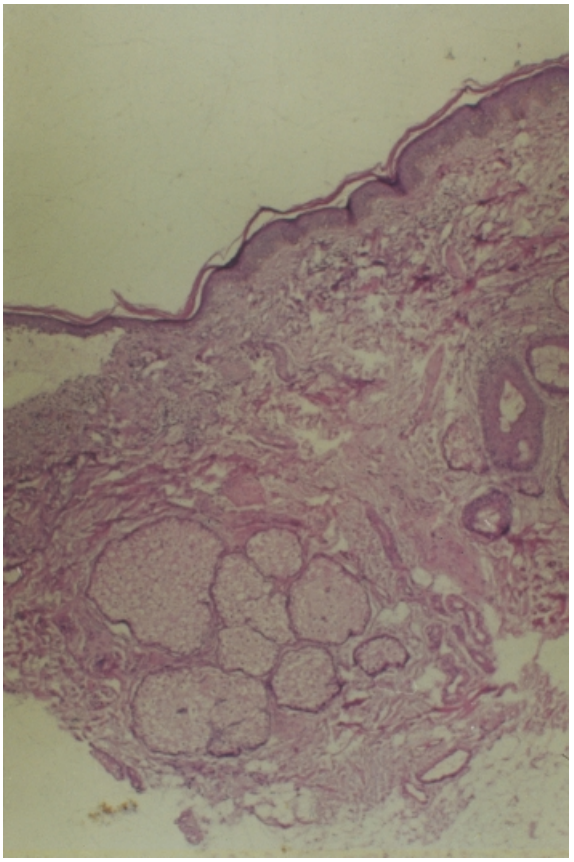

fig. 2 Effacement of rete ridges, minimal collagen homogenization, subepidermal bullae formation and superficial perivascular dermal infiltrate (haematoxylin and eosin, original magnification × 40).

without any other physical abnormalities. Laboratory findings, including complete blood count, peripheral smear, erythrocyte sedimentation rate, fasting blood glucose, liver and renal function tests, urinalysis and thyroid function tests, were in normal ranges. Antibodies against *Borrelia burgdorferi* were negative as was the autoantibody screen. Posteroanterior chest radiography and electrocardiography were normal. Histological examination of a skin biopsy specimen taken from the edge of the lesion confirmed an interface dermatitis with slight epidermal atrophy, hydropic degeneration of basal keratinocytes and effacement of rete ridges. Subepidermal bullae formation, minimal homogenization in collagen bundles in some areas, and elastic fibre degeneration with perivascular mononuclear lymphocytic infiltration accompanied by melanophages in the upper dermis were observed (fig. 2). The man was treated with 30 mg acitretin daily for 2 months. The dosage was tapered to 20 mg after improvement was achieved, and treatment was continued for another 3 months with gradual tapering. The lesions were not completely cleared, but obvious clinical improvement was attained with control of itching and no relapse was noted in 6 months of follow-up.

The cause of LSA is unknown, but genetic susceptibility and autoimmune mechanisms have been suggested.[1,2,8] The occurrence of extragenital lesions has been reported in 15–20% of patients with LSA.[8] To our knowledge, few cases have presented scalp involvement.[5–8] Foulds[7] described a case with pruritic scalp lesions and hair loss associated later with vulvar LSA. Gomez-Calcerrada *et al.*[5] reported another case who developed LSA of the scalp after noticing lesions on the trunk. The previously reported cases were females, but our patient was a male. One of the distinctive features of our case was the localization solely on the scalp without genital or other extragenital involvement. The annular configuration of the lesions in our case was also unusual; this configuration was seen in one other case reported by Patel and Reed.[10]

Bullous and haemorrhagic lesions have been described in LSA.[3,5] Although histological examination revealed subepidermal bullae in our case, we did not observe bullae formation clinically, probably because of suppression due to previously administered treatments. The lesions could have been provoked by trauma, from rubbing, as well as solar radiation.

Extragenital LSA must be differentiated from morphoea and atrophic lichen planus.[2] Association with lupus erythematosus, alopecia areata, vitiligo and other autoimmune diseases have been reported.[1,2] We excluded diagnoses of morphoea, lichen planus, discoid lupus erythematosus, porokeratosis and sarcoidosis by laboratory and histopathological findings.

The clinical course of LSA is variable and choice of treatment is still controversial. The use of oral retinoids in LSA has recently been shown to achieve satisfactory improvement.[9] However, there have been no long-term studies on the treatment of extragenital LSA, although acitretin treatment gave excellent results in our case, with the disappearance of pruritus and manifest clinical improvement of the lesions. We propose that scalp involvement may be a presenting sign of LSA, and oral acitretin is a useful treatment in cases of scalp lesions unresponsive to topical therapies.

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Palmar telangiectases and lung carcinoma: a possible association?

To the Editor

A 63-year-old patient was referred because of a sudden asymptomatic palmar eruption, which appeared 2 months earlier. On examination telangiectases were found on the palms only, without involvement of the rest of the body (fig. 1). The rest of the physical examination was unremarkable.

Routine blood and urinalysis tests, antinuclear factor and serum immunoglobulins were normal. Skin biopsy revealed slight dilated blood vessels in the upper dermis. Chest X-ray and computed tomography examinations revealed a right lung mass in the middle lobe. A lung biopsy was done and revealed non-small cell carcinoma, predominantly squamous cell carcinoma with poor to moderate differentiation, with areas of adenocarcinoma. The patient was treated by chemotherapy but the patient died 2 months later.

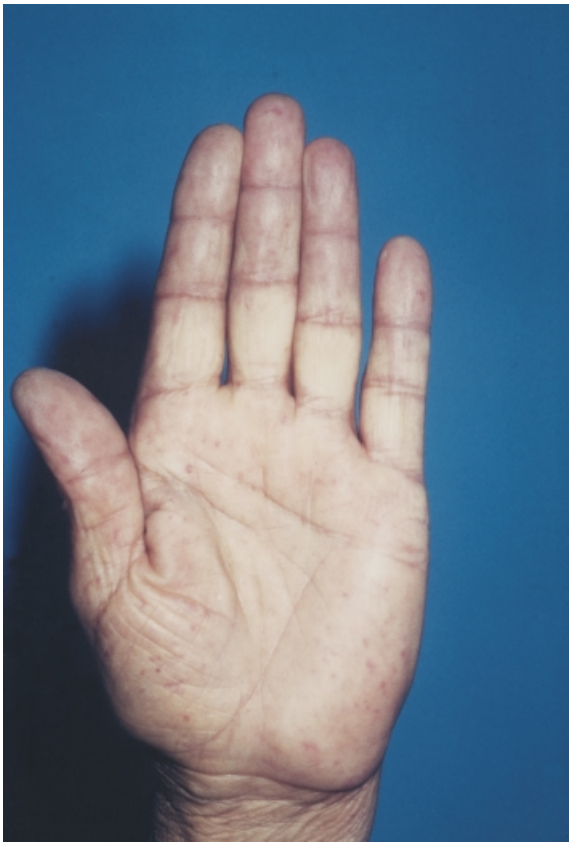

fig. 1 Palmar telangiectases.

Telangiectases are permanent dilatation of blood capillaries and are considered a normal cutaneous finding, it may appear in sun-exposed areas and may appear also in several skin and systemic diseases, including rosacea, basal cell carcinoma, discoid lupus erythematosus and other collagen vascular diseases and congenital diseases (Table 1).

Table 1 Causes of telangiectases

Skin diseases
Rosacea, actinic damage, basal cell carcinoma, poikiloderma, discoid lupus erythematosus, sarcoid, lupus vulgaris
Systemic diseases
Collagen vascular diseases: systemic lupus erythematosus, scleroderma, dermatomyositis
Congenital disease: hereditary benign telangiectasia, ataxia telangiectasia, Bloom syndrome, Cockayne's syndrome
Miscellaneous
AIDS, cardiac myxoma, pulmonary diseases, internal malignancies, exposure to aluminium
Pregnancy
Drug related
oral contraceptive, calcium channel blockers

Eruptive telangiectases may be drug induced or related to internal diseases, such as systemic lupus erythematosus, cardiac myxoma, pulmonary diseases and exposure to aluminium. Eruptive telangiectases has also been reported rarely in internal malignancies. Only few case reports presenting this relationship have been published and include angiotropic lymphoma[1] and ovarian[2] and bronchogenic[3] carcinoma.

The association between palmar telangiectases and lung carcinoma is not well established but it is recommended that neoplastic disease in patients with eruptive telangiectases without internal disease or drug-related history should be ruled out.

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Topical immunotherapy with squaric acid dibutylester: unusual hair pigmentary changes in two cases of alopecia areata

To the Editor

Topical immunotherapy (TIT) with potent contact sensitizers has long since been the therapeutic approach to alopecia areata and viral warts recalcitrant to first-line treatment.[1,2] Considering the significant response rates obtained in such, often otherwise intractable conditions, TIT appears to be an obvious example of how delayed hypersensitivity can be exploited to beneficial effect.

Two females aged 24 and 27 years, respectively, were referred to us for treatment of a 3- and 4-year history, respectively, of recalcitrant alopecia areata totalis. After nearly a 6-month course of TIT with squaric acid dibutylester, a clinical response was obtained, with patchy regrowth of terminal dark-coloured hair. The remarkable feature of these cases is that the patients, both of a fair skinned, were, respectively, blonde and red haired prior to the onset of the disease. At the time of writing the dark regrowth is unchanged, while both the perifollicular skin in the scalp, and the hair all over the rest of the body surface retain their natural coloration.

Table 1 Untoward effects observed under topical immunotherapy[3]

Local severe pruritus or bullous eruptions
Contact urticaria
Facial or eyelid swelling
Generalized eczema or urticaria
Erythema multiforme-like reactions
Persistent, prurigo-like eruptions
(Angelini G, Mastrolonardo M, unpublished observation)
local hyper- or hypopigmentation regional lymphadenopathy
Fever, headache, palpitations and flu-like symptoms

TIT is often the last resort for the management of serious conditions refractory to other treatments. However, the considerable array of potential untoward effects (Table 1)[3] (Angelini G, Mastrolonardo M, unpublished observation) makes its use by inexperienced personnel, or in inadequately selected cases inadvisable. Among sequelae of TIT, dyschromic changes have been reported to involve the skin, with hypo- or hyperpigmented patches at the treatment site. Instead, no significant effects have been described on hair pigmentation, apart from the fact that the regrowing shafts are often initially white.

The cases reported herein seemed worth presenting for the singular pigmentary metamorphosis observed in the newly grown scalp hair. To the best of our knowledge, such a puzzling effect of TIT has never been described in the literature, and the reasons for this phenomenon remain obscure. The only certainty in the matter is that our patients are very happy to have to go back to their hairdressers!

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Red fingers syndrome associated with hepatitis C virus

To the Editor

Red fingers syndrome has been rarely described in human immunodeficiency virus (HIV)-negative patients. We here report a case of red fingers syndrome in a patient with hepatitis C virus (HCV) infection.

A 42-year-old Caucasian woman was admitted for evaluation of a 8-month history of painless acral erythema. History disclosed a chronic alcohol intoxication, an opiate addiction and a benzodiazepine dependency. At examination, the patient showed a distal erythema on the dorsal aspect of the fingers and the toes (fig. 1). In addition, she had spider angiomas, telangiectases on the face, trunk and arms, a palmar erythema, and a glossitis with an atrophic red and smooth tongue. The patient did not exhibit photosensitivity or Raynaud's syndrome.

Liver tests revealed an increased level of the γ-glutamyltransferase to 126 U/L (normal < 35). C-reactive protein, fibrinogen, platelet count, prothrombin time and factor V were within normal limits. Antinuclear antibodies and cryoglobulinaemia were not detected. Serological tests for hepatitis B virus and for HIV 1 and 2 were negative. In contrast, she had evidence of an HCV infection with positive serological tests. Blood screens for opiates and benzodiazepines were positive.

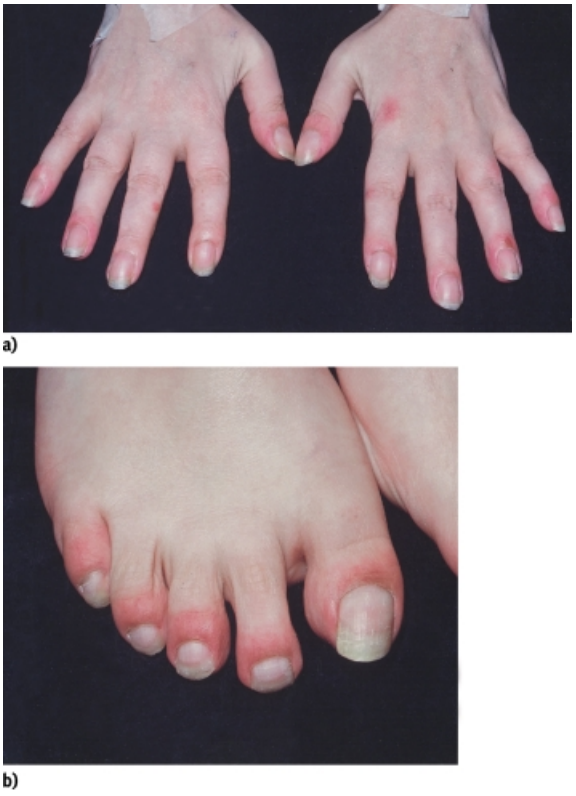

fig. 1 The distal erythema on the fingers (a) and the toes (b) was well demarcated with fine periungual telangiectases.

Red fingers syndrome is defined as a chronic, painless, well-delimited erythema of all the fingers and the toes with multiple periungual telangiectases of at least 1 month duration.[1–3] Histological examination of cutaneous lesions typically shows dilatation of the capillaries and of the postcapillary venules.[2,4]

The prevalence of red fingers syndrome has been estimated to be less than 0.1% in a general dermatology clinic.[3] In contrast, this syndrome is not rare in HIV-infected patients with hepatitis C.[1,3] In fact, in 400 consecutive HIV-positive patients, 28 patients (7%) were recently found to have red fingers syndrome.[3] Noteworthy, 27 of these 28 patients (96%) also had serological tests for HCV infection with evidence of an active hepatitis.[3] In addition, almost all HIV-positive patients with red fingers syndrome appear to be intravenous drug abusers.[2] The frequent use of benzodiazepines at the time of diagnosis has also been observed in one study.[2] Finally, HCV infection is very rarely found in patients with red fingers syndrome in the absence of concomitant HIV infection, such as in our patient.[2–4]

It is likely that red fingers syndrome results from small-vessel alterations due to liver diseases associated with viral infections, HIV infection, and for immunological disturbances, such as cryoglobulinaemia.[2,4] Interestingly, necrolytic acral erythema, another recently described disorder, is also strongly associated with HCV infection.[5] The latter is characterized by well-defined, tender, dusky, erythematous lesions with blisters on the dorsa of the feet and sometimes on the hands.[5] This condition, in which neither antinuclear antibodies nor cryoglobulinaemia are found, can be successfully treated with interferon α and zinc.[5] These observations provide additional support to the idea that HCV has a direct or indirect role in the development of capillary disorders involving acral sites.

A periungual erythema that is not a painless, well-delimited erythema of all the fingers and the toes of at least 1-month duration does not meet the criteria of red fingers syndrome and is not specific of HIV and HCV infections.[3,6] The differential diagnosis of red fingers syndrome includes, besides necrolytic acral erythema, connective tissue diseases such as dermatomyositis or systemic lupus erythematosus, chilblains, drug-induced acral erythema and Harms' syndrome (papular–purpuric gloves and socks syndrome).[7] Medical history, clinical features and laboratory findings can establish the diagnosis in these cases.

No specific treatment is available for the management of the red fingers syndrome. Nevertheless, our observation suggests that recognition of this syndrome is important as it is frequently a cutaneous marker for HCV and HIV infection, for which early and specific treatments are mandatory. Hence, serological tests for HIV and viral hepatitis as well as liver tests are mandatory in patients with this syndrome.[3]

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