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Spitz naevus showing clinical features of both granuloma pyogenicum and pigmented naevus

SIR, Spitz naevus is a benign melanocytic lesion that shares many histological features with malignant melanoma.[1] It is most common on the lower extremities and the face of children, and presents at birth only rarely. Spitz naevi most commonly appear as solitary, pinkish, asymptomatic, dome-shaped, round to oval, firm nodules, most of which are light-coloured and soft, and may be clinically diagnosed as granuloma pyogenicum, haemangioma or dermal naevus.[2] However, pigmented Spitz naevus, or the dark-coloured type, may be tan, brown, or even black, and thus should be differentiated from malignant melanoma and pigmented naevus.[2]

A 16-month-old Korean boy presented with a 4-month history of a 0·5 × 0·5 × 0·5 cm pinkish-coloured eroded dome-shaped nodule arising on a 1·2 × 0·5 cm congenital verrucous, blackish plaque on the left side of the chest (Fig. 1a). Excisional biopsy was performed. Microscopy of the pinkish nodule showed many clusters of atypical melanocytes and increased numbers of vessels in the oedematous dermis. The lesional cells were smaller in size with increasing depth. In the centre of the verrucous, blackish plaque, there was symmetrical, well circumscribed, infiltration of atypical melanocytes in the upper dermis. There were also collections of melanophages and infiltration of lymphohistiocytes in the dermis. In the periphery of the verrucous plaque, there were nests of atypical melanocytes with some mitotic activity within the epidermis and in the dermis, with moderate melanin pigmentation. The nests were composed of spindle cells and epithelioid cells. Clefts were observed between nests of melanocytes and keratinocytes (Fig. 1b). On immunohistochemical staining, the nest cells in the verrucous plaque were positive for HMB-45, but those in the dome-shaped nodule were negative. They were all positive for S-100 protein. A diagnosis of Spitz naevus was made, and the patient has been followed up for 6 months after excision without any evidence of recurrence.

The Spitz naevus was first described in 1948 by Spitz,[3] who also established histological criteria for differentiating Spitz naevus from malignant melanoma. Most Spitz naevi are seen during the first two decades of life,[2,4] but they are rarely present at birth.[2] The trunk, as in our patient, is considered in most studies to be a rare site.[5–7] However, one study of 211 patients found that most lesions (39%) were located on the trunk.[8] In general, the clinical appearance of Spitz naevi can be divided into four basic types: (i) light-coloured and soft (usually smooth, pink, or slightly pigmented and may also resemble granuloma pyogenicum or haemangioma); (ii) light-coloured and hard (resemble a dermatofibroma or small keloid); (iii) dark-coloured (less common and vary in degree of pigmentation; more darkly pigmented lesions occur less frequently); and (iv) multiple or aggregated lesions.[1] In our patient, the initial lesion was black, and the subsequent lesion

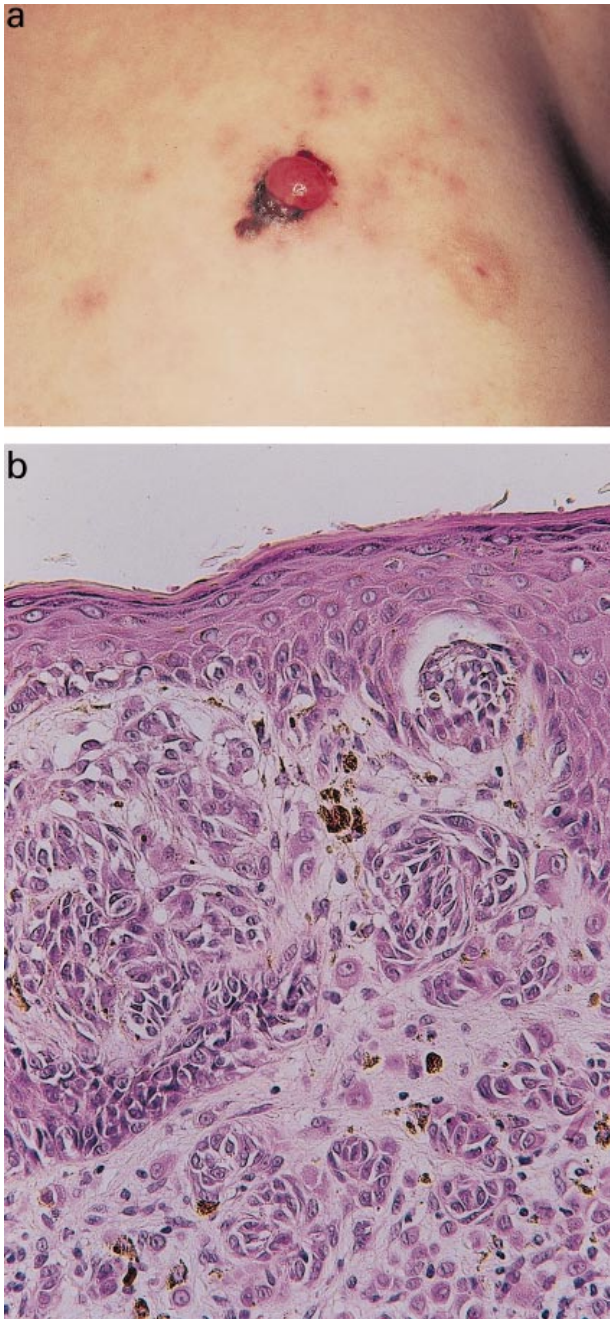

Figure 1. (a) A pinkish dome-shaped nodule with an eroded surface, arising on a verrucous, blackish plaque on the left side of the chest. (b) In the verrucous component of the lesion, there are nests of melanocytes within the epidermis and in the dermis. The nests are composed of spindle cells and epithelioid cells. Note the cleft between nests of melanocytes and keratinocytes (haematoxylin and eosin; original magnification × 400).

arising from the initial lesion was pinkish and soft. To our knowledge, combined dark-coloured and light-coloured, soft types of Spitz naevi presenting in one lesion sequentially, as in our patient, have not been described previously.

Histopathologically, they resemble common naevi in terms of their architectural pattern. They are small, symmetrical, and well circumscribed. The epidermal component is arranged in nests that tend to be orientated vertically and, although large, the nests do not vary a great deal in size and shape or tend to become confluent.[2] In melanoma, nests are variable in size, shape and orientation. In Spitz naevi with junctional activity, there are often artefactual clefts above the naevus cells at the epidermal–dermal junction. Rarely seen in melanoma, this represents a useful diagnostic feature.[8] Important cytological features of Spitz naevi include the presence of large spindle cells and epithelioid cells. Spindle cells or epithelioid cells may predominate, or the two types of cells may be intermingled.[2] The cells become smaller in size with increasing depth and look more like the cells of a common naevus.[8] In our patient, the initial verrucous plaque clinically resembled melanocytic naevus and the subsequent soft nodule looked like granuloma pyogenicum. However, the histological findings described above were consistent with Spitz naevi, despite the mixed clinical features of both granuloma pyogenicum and melanocytic naevus in the same lesion.

Immunohistochemical studies in Spitz naevi have shown that S-100 protein staining can be a useful marker in determining the histogenesis of various skin tumours but cannot be used to distinguish between Spitz naevi and melanomas because both display a similar staining pattern.[1] HMB-45 antibody, originally described as specific for malignant melanoma,[9] has shown a similar staining pattern in Spitz naevi to that seen in malignant melanoma in many studies.[10,11] Therefore, it cannot be used to differentiate between Spitz naevi and malignant melanomas. Interestingly, the nest cells in the verrucous plaque were positive for HMB-45, but those in the dome-shaped papule were negative, although they were all positive for S-100 protein.

Spitz naevi are reported to arise in areas of injury, burn, irradiation or vaccination, and they may develop within a hyperpigmented or naevus spilus-like area[12] and within compound naevi.[13] However, in our patient, the clinical and histopathological findings of the verrucous plaque were consistent with Spitz naevus, and there was no history of trauma.

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Efficacy of basiliximab, a chimeric anti-interleukin-2 receptor monoclonal antibody, in a patient with severe chronic atopic dermatitis

Sir, Chronic atopic dermatitis (AD) is characterized by increased expression of activated T cells. Basiliximab is a chimeric (human/mouse) monoclonal antibody[1] that binds to the α chain of the interleukin (IL)-2 receptor (CD25) with an affinity approximating that of IL-2 itself. It is therefore a potent inhibitor of IL-2-mediated T-cell proliferation, and has been shown to be effective in severe psoriasis.[2,3] We report the efficacy of basiliximab in chronic AD.

A 29-year-old Swiss woman had suffered from AD since childhood. All conventional therapies, including topical and systemic steroids, had failed to give benefit. At presentation, her total IgE was > 5000 U mL^{-1}. She also suffered from recurrent herpes simplex virus (HSV) type 1 infections, and intermittent episodes of pyelonephritis.

At presentation, she had very severe chronic AD over her whole body, with lichenification, pruritic excoriation, hypopigmented and hyperpigmented areas, and fine scaling. The severity of her condition was quantified using the SCORAD index.[4] She was commenced on cyclosporin (Neoral®; Novartis, Basel, Switzerland) 150–250 mg daily (maximum dose 5 mg kg^{-1} daily). She continued to apply topical steroids, and to take valaciclovir for prophylaxis of HSV.

Initial response to cyclosporin was good, with reduction in

pruritus and improvement in the skin lesions. However, after 6 weeks she developed a urinary tract infection that required antibiotic treatment and reduction in the cyclosporin dose. As a result her condition deteriorated, with increased pruritus and eczematous activity. Raising the cyclosporin dose again brought her condition under reasonable control, but at the end of nearly 10 months of cyclosporin therapy, her dermatitis had improved by only about 20% from initial presentation.

At this stage, while continuing with cyclosporin 150 mg daily, she was treated with basiliximab (Simulect®; Novartis) 20 mg by intravenous bolus injection, repeated 4 days later. There was an immediate and dramatic improvement in her condition, in terms of both extent and intensity of disease, and of pruritus and sleep deprivation. Her SCORAD index fell from 68·6 prior to the first basiliximab injection to 37·1 on the day of the second injection, and to 14·25 at 2 weeks after completion of basiliximab treatment. Benefits were maintained for a further 2 weeks, after which the SCORAD index began to rise again. No local or systemic adverse events were attributable to basiliximab.

Cyclosporin is effective in patients with chronic severe AD, but response is variable and sometimes disappointing, while the adverse-events profile limits both the daily dose and the duration of treatment. Our patient tolerated cyclosporin reasonably well for nearly 10 months, although only 20% clinical improvement was achieved.

The addition of basiliximab resulted in an immediate and dramatic improvement in her AD. This improvement was maintained for about 4 weeks, after which her dermatitis began to relapse. Although she continued to receive both valaciclovir and cyclosporin 150 mg daily, the timing, degree and duration of the clinical response make it likely that response was due to basiliximab therapy.

Basiliximab was developed primarily for the immunoprophylaxis of solid organ transplantation. Randomized placebo-controlled studies in adult kidney transplant patients have shown that the addition of basiliximab to immunosuppressive therapy with cyclosporin and corticosteroids reduced the incidence of biopsy-confirmed acute rejection episodes by 28–32%, compared with placebo.[5,6] In this context basiliximab was well tolerated, with no evidence of injection site reactions, cytokine release syndrome, anaphylaxis, increased incidence of bacterial or viral infections, post-transplant lymphoproliferative disorder, or new malignancy. The adverse-events profile of basiliximab used long-term at regular intervals has not been established, but is likely on theoretical grounds to be favourable.

Basiliximab suppresses CD25 expression on lymphocytes for 30–45 days, but with no risk of the prolonged immunosuppression associated with antilymphocyte preparations.[7,8] The duration of response to basiliximab seen in our patient, about 30 days, is compatible with this activity and with the known half-life of the agent.

We have shown that the addition of basiliximab to low-dose cyclosporin can achieve rapid and clinically significant improvement in a patient with severe chronic AD. Suppression of the IL-2 receptor by monoclonal antibody therapy may therefore represent a significant advance in the management of this condition.

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Treatment of atopic dermatitis with mycophenolate mofetil

SIR, We would like to reply to the letter of Hansen *et al.*[1] regarding the use of mycophenolate mofetil (MMF) in atopic dermatitis (AD). The authors treated five patients with moderate to severe AD with MMF 1.0–1.25 g twice daily for up to 12 weeks. However, only two patients had slight improvement, as determined by SCORAD index, while three patients did not respond at all. These observations are in

contrast to results in two open studies: in one study all of 10 patients with AD responded to MMF treatment with a mean reduction in SCORAD index of 68%,[2] while in the second study seven of 10 patients with AD improved with a mean reduction in SCORAD index of 75%[3] (responders only). There are various explanations for these discrepant results, including reporting bias of responders, patient selection, and dose of MMF. Although the patients in the two studies above[2,3] had received at least one previous therapy (conventional topical treatment, oral glucocorticosteroids, phototherapy, cyclosporin or interferon-γ), they had only (if specified) been refractory to one or two, whereas the patients described by Hansen *et al.* had received a mean of 3.4 different systemic treatments. These might therefore be patients in whom any further immunosuppressive therapy might be viewed as likely to fail.

Another explanation for discrepancy is the dose of MMF that was used. The standard MMF dosage in organ transplantation is 2 g daily, but in this situation MMF is always combined with high doses of other immunosuppressive agents. Reports on the use of MMF in inflammatory diseases of the skin recommend a daily dose of 2.0–2.5 g.[4] However, in a study by Jones *et al.* the parent compound mycophenolic acid was effective in reducing or clearing psoriasis at the mean dosage of MMF 3.6 g daily.[5] It is therefore reasonable to conclude that some patients need higher concentrations of MMF for successful therapeutic response, as observed for other immunosuppressants such as cyclosporin. The non-responsiveness of the patients described by Hansen *et al.* may indicate that they belong to a severely affected subpopulation who need either higher doses of MMF or immunosuppressive combination therapies.

The current literature shows that a considerable proportion of patients with eczema benefits from MMF therapy. So far, only a small number of patients has developed severe unwanted effects. Therefore randomized controlled clinical trials should be performed, including a number of patients with a range of doses of MMF and careful patient selection to ensure equivalent groups in terms of previous therapy.

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A comparison of the effect of narrow-band ultraviolet B in the treatment of psoriasis after salt-water baths and after 8-methoxypsoralen baths

Sir, There is a disparity between the absorption spectrum of 8-methoxypsoralen (8-MOP) and the ultraviolet (UV) action spectrum for psoralen-sensitized erythema. In an action spectrum corrected for unsensitized reaction, 313- and 365-nm UV radiation have similar efficacies.[1–4] Ortel *et al.* therefore evaluated the relative erythemogenic and antipsoriatic efficacy of narrow-band (311-nm) UVB with and without prior psoralen exposure.[5] They discovered that the efficacy of 311-nm UVB could be enhanced by psoralen taken orally or delivered topically by bath water. Sakuntabhai *et al.* described a pilot study in which they showed that psoriatic lesions on the arms in eight of nine patients disappeared faster after taking 8-MOP followed by 311-nm UVB compared with 311-nm UVB only.[6] The same group then compared (oral) psoralen-UVB (311 nm) and psoralen-UVA photochemotherapy (PUVA) in the treatment of 100 patients with psoriasis.[7] After 15 treatments with UVB, 43 of 50 patients were without psoriatic lesions and after a mean of 16·5 treatments with UVA, 37 of 50 patients had cleared.

In the Psoriasis Day Care Centre at Ede most patients with psoriasis are treated with a relaxing salt bath prior to irradiation with narrow-band 311-nm UVB. In a minority of cases this treatment modality does not lead to satisfactory clinical results. The therapy for this subgroup is then changed to bathwater PUVA. On the basis of the above studies we therefore queried whether our 'gold standard therapy' could be improved by adding 8-MOP instead of salt to the bath water.

Forty patients participated in this study after having given informed consent. They were randomized to receive either a salt bath prior to irradiation with narrow-band 311-nm UVB (salt-UVB group) or a psoralen bath prior to irradiation with 311-nm UVB (psoralen-UVB group). The mean age in the salt-UVB group was 41 years (range 18–86) and in the psoralen-UVB group was 49 years (range 18–77). In the salt-UVB group 15 patients had skin type II, three patients skin type III and two skin type IV; in the psoralen-UVB group these numbers were respectively 14, four and two. Exclusion criteria were pregnancy, age younger than 18 years, use of systemic photosensitizing agents, treatment with UVB, PUVA, systemic immunosuppressants or antimetabolites within 6 weeks, and topically administered antipsoriatics within 2 weeks before entering the study. All patients were allowed to use an emollient cream if necessary.

Baths were prepared by dissolving 1 kg of NaCl (salt-UVB group) or a 0·5% ethanolic solution of crystalline 8-MOP

(psoralen-UVB group) in tap water at 36–38 °C to give a final concentration of 6·7 g L^{-1} NaCl or 5·7 mg L^{-1} 8-MOP. Patients were immersed for 15–20 min, gently dried and immediately irradiated. Thirty-two Philips TL01/1000 W tubes in a Waldmann UV 1000 unit (Waldmann, Villingen-Schwenningen, Germany) were used for narrow-band 311-nm UVB irradiation. Radiation measurements were taken with a Waldmann UV meter. The irradiance was 7·3 mW cm^{-2}.

Determining the minimal erythema dose (MED) or the minimal phototoxic dose (MPD) evaluated individual photosensitivity. The MED and MPD were determined according to standard procedures by visual assessment of a threshold reaction.[3] Readings for both MED and MPD were performed at 24 and 72 h.

At the beginning of the study, the Psoriasis Area and Severity Index (PASI) was calculated on the arms, trunk and legs (max. 64·8). All patients were suffering from psoriasis vulgaris with subacute exacerbation. The whole body, except the head, was irradiated with 70% of the MED or MPD and this dose was increased by 30% at subsequent treatments. The maximal time of 311-nm UVB exposure was 8 min for skin type II, 10 min for skin type III and 12 min for skin type IV. Irradiations were given on Monday, Wednesday and Friday; at every six treatments, the PASI was calculated again until either a score of 0 was reached or the patient had had 24 treatments.

In the salt-UVB group, four patients dropped out: one had been included while on methotrexate medication, one had been given a prescription for calcipotriol ointment during the study and in two cases the PASI was lost or incorrectly entered into the computer. In the psoralen-UVB group, three patients dropped out: one had to be hospitalized during the study for a non-psoriasis-related disease, for unknown reasons one did not show up after six treatments and in one the PASI was lost (as above). In each group, two patients (each on a single occasion) developed burning erythema with small blisters on the protruding parts of the body (breast, hip etc.) on the second day after the last irradiation.

In the salt-UVB group, the mean ± SD PASI (excluding the head) was 14·6 ± 6·1 at the beginning, 8·3 ± 3·6 after 2 weeks, 3·5 ± 2·4 after 4 weeks, 1·5 ± 1·0 after 6 weeks and 0·4 ± 0·6 after 8 weeks of treatment. Complete clearance was achieved after 4 weeks in one patient, after 6 weeks in two patients and after 8 weeks in eight patients. In the psoralen-UVB group, the mean ± SD PASI (excluding the head) was 11·9 ± 5·9 at the beginning, 7·8 ± 6·9 after 2 weeks, 5·1 ± 5·9 after 4 weeks, 3·1 ± 5·1 after 6 weeks and 1·4 ± 2·9 after 8 weeks of treatment. Complete clearance was achieved after 4 weeks in one patient, after 6 weeks in three patients and after 8 weeks in six patients.

Six weeks after having received a salt bath prior to irradiation with narrow-band 311-nm UVB three times weekly, the mean PASI dropped from 14·6 to 1·5 ($n = 16$). It took 8 weeks to achieve the same clinical results using psoralen baths prior to irradiation with narrow-band 311-nm UVB three times weekly; the mean PASI dropped from 11·9 to 1·4 ($n = 17$). Hence there seems to be no benefit in adding psoralens to the bath water prior to 311-nm UVB treatment.

Why do our results differ from the promising results of Ortel *et al.*?[5] Several reasons can be proposed. Firstly, the study design and number of participating patients differed. In the 'three subgroups' study of Ortel *et al.*, the therapeutic efficacy of 311-nm UVB with and without oral psoralen in one group ($n = 5$) was assessed without using the PASI. In these five patients the erythemogenic and therapeutic efficacy of 311-nm UVB was increased by oral psoralens. The second group ($n = 10$) received UVA (one side) and 311-nm UVB (other side) after oral psoralen. In these 10 patients, also assessed without using the PASI, systemic 8-MOP plus UVA was comparable with systemic 8-MOP plus 311-nm UVB. This result corresponds with the study of de Berker *et al.*,[7] although their study did not mention an objective scoring system for the severity of the psoriasis either and additionally did not count psoriatic lesions on the lower legs when defining clearance. The last subgroup ($n = 11$) was exposed to UVA (one side) and 311-nm UVB (other side) after bath-water exposure to 8-MOP: 311-nm UVB was clearly superior to UVA, as measured by 'earlier improvement and clearing after 18 exposures with cumulative 30·1 J cm^{-2} '. In these small studies 8-MOP was always compared with UVA or narrow-band UVB. In our study 33 patients were evaluated, and in our study design addition of salt to the bath before 311-nm UVB appeared to work better than 8-MOP.

One might argue that our patients did not receive the correct concentration of 8-MOP in their psoriatic plaques. However, this seems very unlikely, as the concentration of 8-MOP in our baths was 5·7 mg L^{-1}, a concentration that has always been used successfully for our patients with psoriasis receiving bath-PUVA.

It would be interesting to compare the effects of a salt bath prior to narrow-band UVB with use of a psoralen bath prior to broad-band UVA in the treatment of psoriasis. However, it has been known for some time that bathing before broad-band UVB increases the efficacy of the treatment compared with 'dry' irradiations, and in this respect it does not matter whether one uses tap water or 4% sodium chloride.[8] Therefore we have to find out whether this is also true for narrow-band UVB before any further comparison studies are performed.

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Successful ultraviolet A1 treatment of cutaneous sarcoidosis

Sir, We report a 63-year-old woman who presented with a 4 × 2 cm red-brown coloured plaque on her forehead of more than 30 years' duration (Fig. 1a). The plaque had been surgically removed in 1977, but subsequently relapsed and grew slowly (the original histology was unobtainable). Histological examination of a skin biopsy revealed a dense histiocytic infiltrate and 'naked' or sarcoidal granulomas in all parts of the dermis, leading to the diagnosis of sarcoidosis (Boeck's disease). Investigations including X-ray of the chest and hand, ultrasound scan, blood tests (angiotensin-converting enzyme) and ophthalmological examination gave no evidence of systemic involvement.

Treatment with a corticosteroid ointment (mometasone furoate) once daily for 14 days was ineffective, so we used ultraviolet (UV) A1 for this lesion (Dermalight ultrA 1, Dr Hoenle, Martinsreid, Germany; skin surface irradiance 80 mW cm^{-2}), starting with 20 J cm^{-2} for 2 days, 50 J cm^{-2} for 3 days, then 90 J cm^{-2} for 5 days. The final dose of 130 J cm^{-2} was given four times weekly with the surrounding tissue covered. The treatment was well tolerated. After 25 treatment days and a total dose of 2460 J cm^{-2}, the lesion disappeared leaving only a few markedly flattened papules behind (Fig. 1b).

No further biopsy was taken and no further UVA1 treatment was given due to personal reasons of the patient. She was seen in our outpatient clinic for a further 2 months and treated with a corticosteroid ointment (Prednicarbat, Hoechst Marion Roussel, Bad Soden, Germany). No relapse occurred.

Therapy of sarcoidosis is dependent on the distribution of cutaneous lesions and the involvement of internal organs. Whereas limited and flat cutaneous lesions can be treated by injection or topical application of corticosteroids, systemic therapy is recommended for nodular sarcoidosis or for widespread distribution of lesions. Chloroquine, methotrexate, allopurinol, isotretinoin and thalidomide have all been used.[1–6]

UVA1 therapy (340–440 nm) has become an established therapy in severe atopic dermatitis and morphea.[7] Moreover, such disparate diseases as urticaria pigmentosa, lupus erythematosus and acne have been treated with success. Various immunomodulating and immunosuppressive effects of UVA1 are known which may be responsible for the efficacy in this case: long-wave UVA induces apoptosis in T cells, leading to a decreased immune response in inflammatory diseases.[8] Furthermore, UVA1 irradiation causes a decrease in tumour necrosis factor (TNF)-α and an increase in interleukin (IL)-10 in human skin.[9] Sarcoidosis is characterized by an increased production of T-helper 1-type cytokines including TNF-α, interferon-γ and IL-2.[10] IL-10 secretion by macrophages is increased.[11]

Publications on positive effects of radiation therapy in sarcoidosis are rare. Courtois *et al.*[12] and Patterson and Fitzwater[13] described a significant improvement by psoralen plus UVA therapy in cutaneous sarcoidosis. Reported benefit of UVA1 therapy in other granulomatous diseases such as granuloma annulare supported the use of this treatment for our patient. It was not only well tolerated but led to a

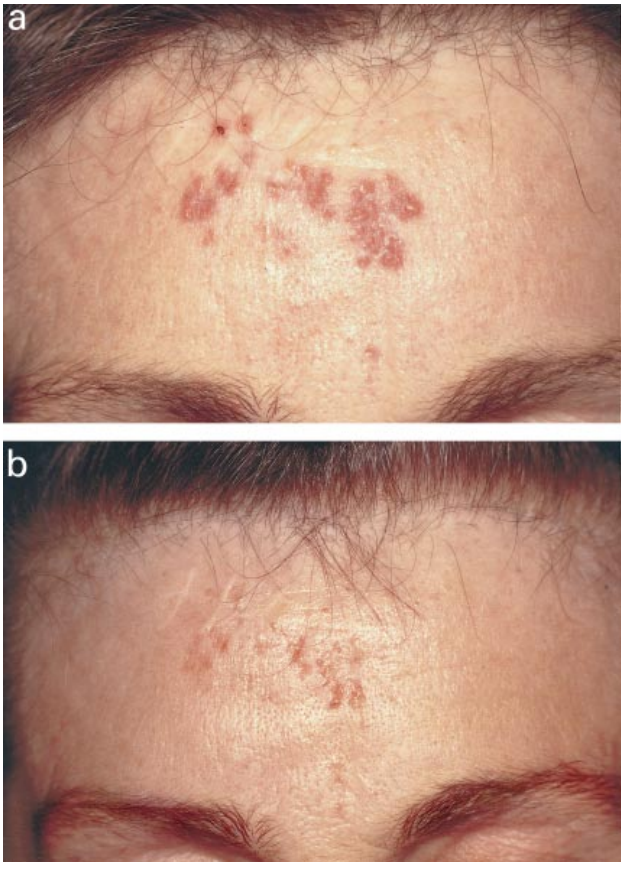

Figure 1. (a) Cutaneous sarcoidosis on the forehead in a 63-year-old woman. (b) Findings after 25 treatments with ultraviolet A1.

significant clinical improvement. However, we cannot exclude spontaneous regression, although the long duration of the lesion makes this unlikely.

Based on this experience, UVA1 therapy may be a promising and effective way of treating cutaneous sarcoidosis, with minor side-effects. Further controlled studies of UVA1 treatment of cutaneous sarcoidosis are warranted.

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Eczéma craquelé resulting from acute oedema: a report of seven cases

SIR, Under the term 'acute oedema blisters' we have recently described the development of bullae in response to rapid accumulation of oedema fluid, usually in a dependent limb.[1] Another response to acute oedema, again seen regularly in clinical practice but poorly described in dermatology texts, is the formation of superficial eczéma craquelé-like crazing and fissuring of skin overlying the oedema. We describe seven representative cases to promote recognition of this entity that we believe occurs when dermal oedema accumulates rapidly and then responds quickly and completely when the oedema resolves.

The seven patients (three females and four males), age range 42–82 years, median age 52 years, were all hospitalized at the time of presentation, and had all developed acute oedema (Table 1). All subjects had temporary impairment of mobility. None had a history of atopic or thyroid disease. The eruption was localized to the site(s) of acute oedema, which in all cases involved the lower extremities with a particular predilection for the ankle and dorsum of the foot. It began with crazing and scaling of the epidermis (Fig. 1a; case 1), closely resembling eczéma craquelé. As the scaling responded to emollient therapy, the underlying pattern of linear or reticulate fissuring and erythema became more apparent (Fig. 1b; case 2). Koebnerization along a surgical wound was noted in one subject (Fig. 1a; case 1). Scattered fine petechial haemorrhage within the fissures was observed in one patient (case 4); more pronounced fine linear haemorrhages along the fissures were seen in two more (case 5, Fig. 2 and case 7). In one subject (case 6) the eczéma craquelé changes were associated with tense blisters affecting the dorsum of the right foot. Mild pruritus was experienced by all patients. Symptomatic relief was obtained with emollients and mild topical corticosteroid preparations, but resolution of the cutaneous signs occurred only as the patients' oedema improved, either due to improved mobility (cases 1–3), treatment of associated cellulitis and leg swelling (case 5) or correction of fluid overload (cases 4, 6 and 7).

The term eczéma craquelé is used to describe the 'crazy paving' or 'crazed porcelain glaze' appearance of the skin surface following desiccation and fracturing of the stratum corneum. Disturbance of the normal epidermal water barrier is thought to be central to this clinical picture,[2] which may result from a combination of factors including decreased sweat and sebaceous gland activity, low environmental humidity and a genetic predisposition to 'dry skin'. The degreasing effects of harsh soaps and excessive skin washing may play a part, particularly in elderly, bedridden hospital inpatients. Eczéma craquelé may also be seen as a component of some forms of dermatitis, particularly nummular dermatitis, and in association with underlying systemic disease including malignancy, myxoedema and nutritional deficiency, when it may be widespread and resistant to standard therapy.[3–5]

In a previous report we described the formation of bullae on the lower limbs following rapid accumulation of oedema fluid and termed such bullae 'acute oedema blisters'.[1] Swift and complete resolution of signs was observed on successful treatment of the leg swelling. We believe that the eczéma craquelé-like changes we describe in this report arise in similar circumstances and result from disruption of the integrity of the epidermal water barrier due to rapid distension of the stratum corneum. In contrast to our cases of 'acute oedema blisters'

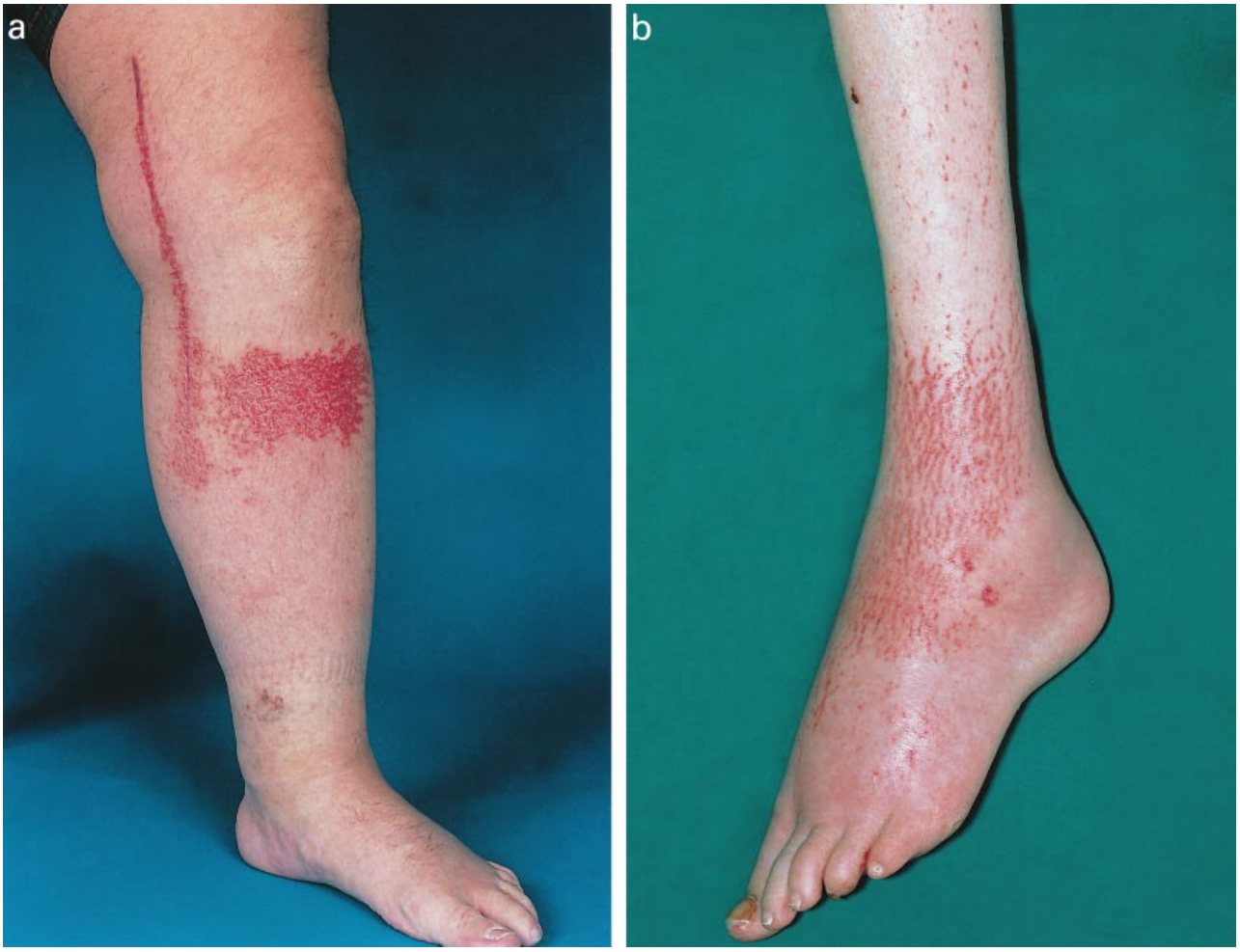

Figure 1. (a) Eczéma craquelé associated with acute cutaneous oedema following surgery (case 1); note the isomorphic phenomenon in the scar. (b) Linear crazing and erythema of the skin following acute oedema of the foot and lower leg (case 2).

where the majority of affected patients were elderly (mean age 74 years) and chronically immobile, the patients who developed eczéma craquelé were generally younger and all had only temporarily impaired mobility; to date we have only seen the coexistence of bullae and eczéma craquelé in one patient with acute oedema.

It is surprising that the clinical picture we describe has hitherto received little attention. In 1970 Caplan recognized that superficial fissuring of the skin occurred 'under clinical circumstances in which xerosis and oedema are prominent', reporting nine such patients under the term 'Superficial Hemorrhagic Fissures of the Skin' and emphasizing that the fine linear haemorrhages he observed within the fissures were not due to an underlying haematological abnormality.[6] He demonstrated by histology that the fissuring might involve only the stratum corneum or could extend to the papillary dermis and thus directly disrupt dermal papillary capillaries. We also observed such linear haemorrhages in two patients and a few scattered petechiae within the fissures in a third. Although Caplan recognized that oedema was important, and indeed demonstrated its presence in his microscopic studies, he hypothesized that the initial event was excessive water loss from keratin followed by splitting of the stratum corneum. By contrast, we believe that the fissuring of the stratum corneum and epidermis is likely to be a direct result of distension from rapid accumulation of cutaneous oedema. It is important to recognize this entity of eczéma craquelé resulting from acute oedema as the clinical signs resolve quickly and completely in response to reduction of the fluid accumulation.

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Table 1. Clinical details of patients with eczéma craquelé associated with acute oedema

No.	Sex	Age	Precipitating cause	Presentation	Resolution of signs?	Impaired mobility?
1	M	55	Acute oedema of tissues around left knee following popliteal aneurysm repair	Eczéma craquelé below left knee and along surgical scar left medial thigh and knee	Yes – with increase in mobility, emollient and mild topical steroid	Yes
2	F	42	Acute oedema of left leg following fractured neck of femur	Linear erythematous eczéma craquelé affecting left ankle and dorsal foot	Yes – with increase in mobility, emollient and mild topical steroid	Yes
3	M	67	Acute dependent oedema due to congestive cardiac failure in patient with ischaemic heart disease	Bilateral eczéma craquelé of lower limbs	Yes – with increase in mobility, emollient and mild topical steroid	Yes
4	F	46	Acute bilateral dependent oedema due to intravenous fluid overload and congestive cardiac failure in patient with longstanding juvenile chronic arthritis and acute septic arthritis of left knee	Bilateral eczéma craquelé of lower limbs more marked on right leg; some petechial haemorrhages seen within fissures	Yes – with correction of fluid overload and reduction of leg oedema	Yes
5	M	82	Acute swelling of right ankle and foot from localized cellulitis	Multiple fine linear haemorrhagic fissures with scaling over dorsum of ankle and foot	Yes – with resolution of cellulitis	Yes
6	F	47	Acute generalized oedema following reduction in diuretic dose in patient with alcohol-related liver disease	Eczéma craquelé of abdomen and upper and lower limbs together with blistering of right foot	Yes – with correction of fluid overload and dose of diuretic	Yes
7	M	52	Acute-on-chronic oedema following exacerbation of congestive cardiac failure	Eczéma craquelé with haemorrhagic changes affecting lateral aspects of both lower limbs	Yes – with correction of fluid overload, emollient and mild topical steroid	Yes

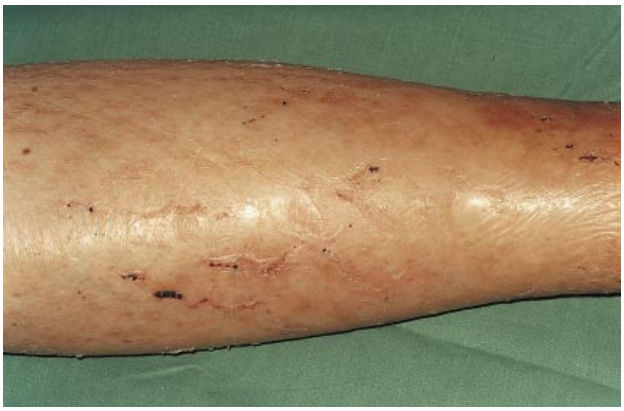

Figure 2. Linear haemorrhage within the fissures (case 5).

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Linear erythema craquelé due to acute oedema in anorexia nervosa

Sir, We report two Japanese patients with novel cutaneous manifestations that arose after receiving nutritional intravenous infusions for anorexia nervosa.

Patients 1 and 2 were women aged 19 and 24 years, respectively. The former had been suffering from anorexia nervosa since August 1998; the latter since 1995, accompanied by systemic lupus erythematosus. Several days after starting a 1700-kcal diet and 1000 mL peripheral intravenous infusion in patient 1, and intravenous hyperalimentation in patient 2, they developed skin lesions. Examination revealed dryness, severe oedema and numerous linear, reddish or brownish erythematous areas, 2–8 mm in width, on their legs and/or feet with severe pain (Fig. 1). Both had additional non-dermatological symptoms including amenorrhoea, hypothermia, bradycardia, hypotension and muscle weakness. Laboratory data showed decreased white blood cell counts, hypoproteinaemia, hypoalbuminaemia, hypotriglyceridaemia, low blood sugar, low triiodothyronine, low insulin-like growth factor-1 and anaemia. Their weight was about 50% of their ideal, with severe anorexia nervosa. We stopped the infusion of patient 1; the intravenous hyperalimentation of patient 2 had already been discontinued because of a bacterial infection at the site of needle insertion. We gave them 20% albumin and furosemide and treated them with heparinoid and/or Azunol® ointment (0·033% 1,4-dimethyl-7-isopropylazulene, an anti-inflammatory agent) topically. As the oedema decreased, their lesions improved with only residual hyperpigmentation but no scarring or atrophy after 1 month.

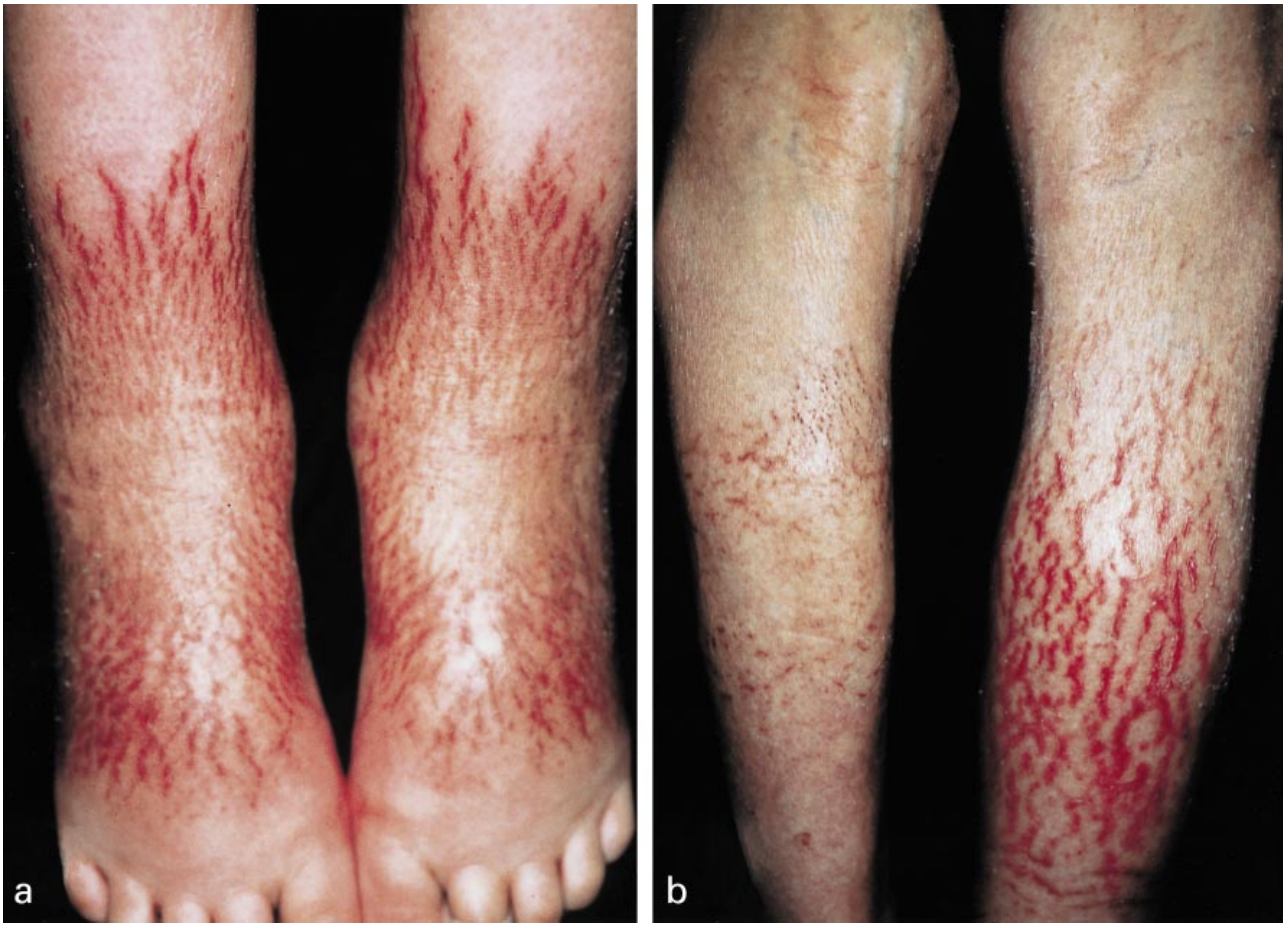

Figure 1. (a) Numerous linear, reddish or brownish lesions on the dorsa of the feet of patient 1. (b) Similar longitudinal erythematous lesions on both legs of patient 2; more lesions are evident on the right leg, which was more oedematous than the left.

Xerosis is a common skin symptom of anorexia nervosa,[1–4] but the lesions in our patients had different clinical features of severe xerosis, exhibiting reticular cracks called the 'crazy-paving' pattern,[5] which generally heal without residual pigmentation. We initially considered these symptoms in our patients as striae distensae because of the direction, which was opposite to the skin distension, but these lesions resolved with no scarring or atrophy. The cracks of xerosis extend through the horny layer to the superficial epidermis, while striae distensae result from damage to dermal connective tissue from stretching. We suspect that the symptoms in our patients resulted from damage to the entire epidermis rather than to the dermis. We have never observed similar symptoms in patients with xerosis and oedema. Therefore these features may be related to anorexia nervosa. When infusions were given based on xerosis and low colloid osmotic pressure due to malnutrition brought on by severe anorexia nervosa, they developed severe oedema for a short period. After that, skin distension occurred primarily over the entire epidermis and the erythematous areas appeared. Thus, these features may be a new cutaneous manifestation.

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Lichenoid vasculitis associated with myeloproliferative disorder: successful treatment with dapsone

SIR, We report a patient with chronic cutaneous vasculitis with an unusual lichenoid appearance, associated with myelofibrosis and an extra copy of chromosome 9. A 69-year-old man presented with a 5-year history of an initially transient skin eruption affecting his thighs, lower legs and ankles. Each attack lasted for several days before subsiding. After 2 years, some of the lesions, particularly those on the lower legs, became fixed, violaceous and flat-topped (Fig. 1). He had a history of carcinoma of the prostate and recurrent deep venous thrombosis. At presentation, he was receiving goserelin injections and long-term warfarin (both of which antedated the eruption by several years).

Examination revealed a palpable purpuric rash typical of small vessel leucocytoclastic vasculitis on his thighs and lower legs, but the eruption around his ankles had a striking lichenoid appearance with a purple colour. Splenomegaly (5 cm below costal margin) was noted but no lymphadenopathy or hepatomegaly. He was afebrile and systemically well. His mucous membranes were normal.

Investigations showed haemoglobin of $14{\cdot}9\ \mathrm{g\ dL^{-1}}$, elevated total white cell count ($25 \times 10^9\ \mathrm{L^{-1}}$), and marked neutrophilia ($23 \times 10^9\ \mathrm{L^{-1}}$; range $2{\cdot}0–7{\cdot}5 \times 10^9$) and a normal platelet count ($146 \times 10^9\ \mathrm{L^{-1}}$). Cytogenetic analysis of bone marrow showed an abnormal karyotype with an extra copy of chromosome 9, in keeping with a myeloproliferative disorder. Renal and liver function tests were normal. Prostatic specific antigen was $0{\cdot}3\ \mu\mathrm{g\ L^{-1}}$ (range 0·0–4·0). Other negative investigations include antinuclear factor, ANCA, and hepatitis B antigen. Bone marrow aspiration produced only a bloody tap, and trephine biopsy showed hypercellularity, increased blast cells, and a moderate excess of reticulin fibres, suggesting myelofibrosis. The leucocyte alkaline phosphatase (LAP) score was elevated, in keeping with this diagnosis.

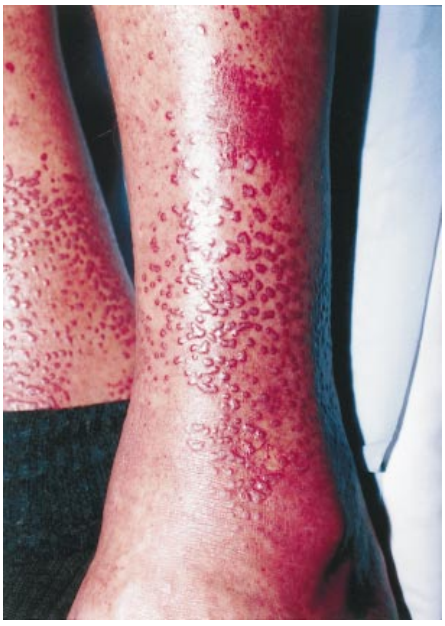

Figure 1. Lichenoid vasculitic rash on lower leg.

Biopsy of both the palpable purpura and the lichenoid papules showed identical features: an active inflammatory process in keeping with leucocytoclastic vasculitis. There were well-defined and localized areas of increased vascularity associated with extravasation of red cells, neutrophil infiltration of the vessel wall and perivascular nuclear dust. Special stains showed extensive haemosiderin deposition within the stroma and fibrin deposition perivascularly. The patient declined a second biopsy for immunofluorescence.

He was started on dapsone 50 mg daily and gentle compression hosiery for the vasculitis. Higher doses of dapsone were not tolerated. This combination resulted in flattening of the papular lichenoid lesions and relieved the discomfort of the rash within 6 months. Subsequently, hydroxyurea 500 mg on alternate days was added for the underlying myeloproliferative disorder. The dose of dapsone was reduced to 50 mg on alternate days with adequate disease control. Although the vasculitis improved, the myelofibrosis had not altered significantly. He remains haematologically stable 18 months after commencing treatment, with the white cell count remaining elevated at around $20 \times 10^9\ \mathrm{L^{-1}}$.

Small vessel vasculitis is a rare but recognized association with myeloproliferative disorders[1] and myelodysplasia,[2] occurring usually before, or less frequently after, the onset of malignancy. Based on data from the American literature, the association of vasculitis occurs significantly more often in haematological disorders than with all other malignancies.[1] Cutaneous vasculitis may antedate the diagnosis of malignancy by 1–38 months. Clinically, there may be palpable purpura, a maculopapular eruption, nodules, urticaria, panniculitis, or even frank ulceration, occurring over the buttocks and legs.[2] A clinically lichenoid eruption with histological features of a leucocytoclastic vasculitis, such as that found in our patient, has not previously been documented. Patients often experience intense pruritus or dysesthesias. Polyarthritis may be present. In one series of 162 patients with myelodysplasia,[2] seven patients (4%) were noted to have cutaneous vasculitis, including leucocytoclastic vasculitis, urticarial vasculitis, and panniculitis. There also appears to be an association between myelofibrosis and SLE in some cases.[2–4] Biochemically, there may be cytopenia in one or more haematological cell lines, and cryoglobulinaemia. Hepatitis B antigen, rheumatoid factor and antinuclear antibodies may be detected. Cytogenetic studies of bone marrow may detect karyotypic abnormalities (which reflects a clonal abnormality) in up to 80% of cases in myelodysplasia and 50% in myelofibrosis. It is speculated that tumour-associated antigens and/or circulating immune complexes may mediate vascular damage.[1]

Non-steroidal anti-inflammatory agents and antihistamines are ineffective, and chemotherapy for the underlying malignancy is inconsistently effective for the cutaneous

vasculitis.[1,5] Corticosteroid therapy may bring about short-term regression in some patients, but carries its own long-term side-effects. Dapsone, an antineutrophilic agent, has been tried in other vasculitides and appears to have been effective even at relatively small doses in our patient.

This correspondence serves as a reminder of the less well-known association of cutaneous vasculitis and myeloproliferative disorder, and reports an unusual and initially confusing lichenoid appearance to some of the lesions.

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Granuloma faciale with extrafacial lesions

Sir, Granuloma faciale is an uncommon chronic dermatosis accepted as a localized form of small-vessel vasculitis. Clinically, it manifests as single or multiple, well-demarcated, red-brown plaques, papules and nodules, nearly always confined to the face. We report a patient with granuloma faciale having multiple extrafacial lesions.

A 47-year-old female farmer presented with persistent mildly pruritic plaques on her face, neck and right arm of 2 months' duration. The first lesions had developed on the ears, then gradually spread to involve the cheeks and neck, and a week previously had spread to the right arm. She had a history of pulmonary tuberculosis 10 years previously and had not been on any medication since then.

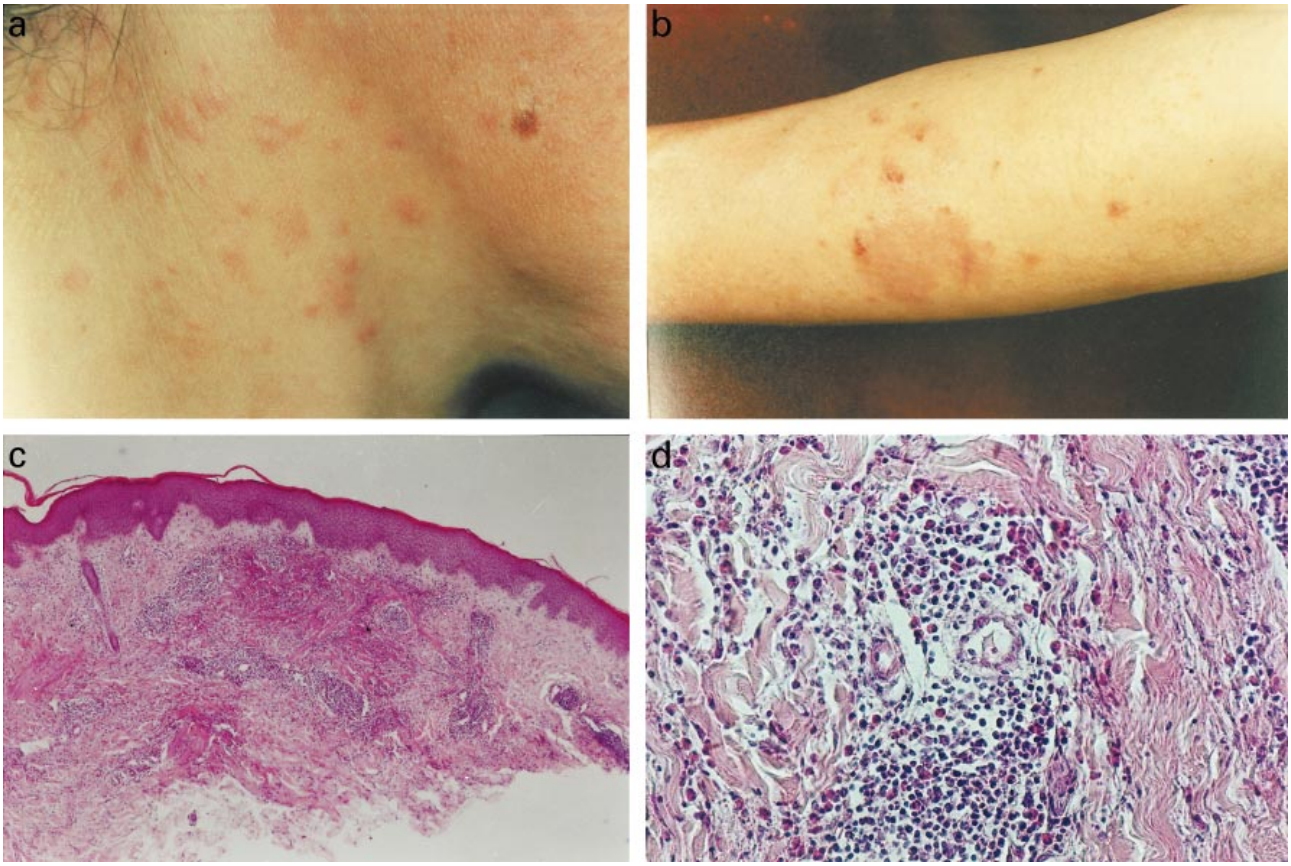

Figure 1. (a) Indurated erythematous papules on the neck; (b) the biggest plaque on the arm; (c) dense mixed infiltrate with a Grenz zone beneath the epidermis (haematoxylin and eosin, original magnification × 20); (d) fibrinoid deposits, nuclear dust, extravasation of erythrocytes around the vessel walls and dense eosinophilic infiltrate (haematoxylin and eosin, original magnification × 200)

Table 1. Cases of extrafacial granuloma faciale

Patient no.	Author	Age (years)	Sex	Facial involvement	Extrafacial localization
1	Lever *et al.*[1]	53	M	+	Trunk
2	Okun *et al.*[2]	54	F	+	Upper extremities
3	Pedace and Perry[3]	45	M	+	Upper extremities
4	Pedace and Perry[3]	47	F	+	Trunk, upper extremities
5	Rusin *et al.*[4]	44	M	+	Trunk
6	Rusin *et al.*[4]	50	F	+	Trunk
7	Frost and Heenan[5]	64	M	+	Scalp, upper extremities
8	Hernandez *et al.*[6]	30	M	+	Trunk
9	Sears *et al.*[7]	57	M	+	Lower extremities
10	Konohana *et al.*[8]	59	M	+	Trunk
11	Kavanagh *et al.*[9]	62	M	–	Scalp
12	Castano *et al.*[10]	51	F	–	Trunk
13	Roustan *et al.*[11]	37	M	+	Trunk, upper extremity
14	Present case	47	F	+	Upper extremity

On examination, there were red-brown, 1–2 cm sized, well-demarcated and slightly indurated nonscaly circular papules and plaques on the face and neck (Fig. 1a). The similar lesions on the right arm coalesced and the largest was about 3 × 2 cm (Fig. 1b). A full blood count, biochemical values, urinalysis and chest X-ray did not reveal any abnormality, including eosinophilia, and general examination was normal.

A skin biopsy from the right arm showed a dense mixed inflammatory infiltrate, not invading the pilosebaceous unit, in the reticular dermis; this was composed mainly of lymphocytes and eosinophils with some histiocytes and neutrophils. Fibrinoid necrosis of vessel walls, nuclear dust and extravasation of erythrocytes around the capillaries were observed. The epidermis was normal except for slight parakeratosis and acanthosis, and there was a Grenz zone between the epidermis and the dermal infiltrate. Broad collagen bundles and fibrosis were also present (Fig. 1c,d). Three weeks later there was a marked improvement with topical mometasone; all lesions disappeared in 6 weeks. During a follow-up period of 6 months, no recurrence was observed.

Granuloma faciale is nearly almost localized to the face, as the name implies. Extrafacial involvement has been reported very rarely (Table 1).[1–11] Apart from two cases,[9,10] facial lesions in all reports coexist and usually precede the extrafacial lesions. Granuloma faciale with extrafacial lesions shows male predominance.

The aetiopathogenesis is unclear, but it was suggested that granuloma faciale may be an Arthus-like immune complex or a gamma-interferon mediated disease.[12] The role of ultraviolet radiation has also been underlined; our patient was a farmer and worked under the sun nearly all day.

Extrafacial granuloma faciale should be differentiated mainly from erythema elevatum diutinum which presents symmetrically on the distal and extensor parts of the extremities. Histologically, fewer eosinophils, absence of Grenz zone, and more dense infiltration distinguishes erythema elevatum diutinum from granuloma faciale.[11]

In conclusion, we present another case of extrafacial granuloma faciale. This disorder should be kept in mind in the differential diagnosis of erythematous indurated papules and plaques on the trunk and extremities.

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Footnote: Işıl İnanir was in Merzifon General Hospital during the observation period.

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Schönlein–Henoch purpura associated with losartan treatment and presence of antineutrophil cytoplasmic antibodies of x specificity

SIR, Schönlein–Henoch purpura (SHP) is a systemic small-vessel vasculitis characterized by vascular deposition of IgA-dominant immune complexes.[1] Although this syndrome characteristically follows an upper respiratory tract infection, drugs have also been implicated as a cause.[2] We report a case of SHP that developed after introduction of losartan, a novel angiotensin II receptor antagonist,[3] and was unusual for its association with antineutrophil cytoplasmic antibodies (ANCA) of x specificity (xANCA).

A 79-year-old caucasian woman was admitted for evaluation of fatigue, arthralgias of the ankles and wrists, and cutaneous purpuric lesions. She also had a chronic obstructive pulmonary disease and cardiac insufficiency with chronic atrial fibrillation, treated with digoxin, acetylsalicylic acid and zolpidem for the previous year. Because of arterial hypertension she was given losartan 4 weeks prior to the development of the symptoms. In addition, she had recently been given mianserin for depression. On examination, she had oedema of the legs and many infiltrated purpuric lesions of up to 2 cm in diameter, located on the lower extremities, ankles, thighs, buttocks and arms. The lesions were in part necrotic with haemorrhagic blisters.

Laboratory examination disclosed an elevated erythrocyte sedimentation rate of 40 mm in the first hour and a C-reactive protein level of 65·8 mg L^{-1} (normal < 10). Full blood count, electrolytes, liver and renal function tests, urine analysis, complement haemolytic activity, C4 and C3 complement levels, protein electrophoresis and immunoelectrophoresis were within normal limits. Serological tests for hepatitis B and C viruses, parvovirus B19 and mycoplasma were negative. A search for cryoglobulins, antinuclear antibodies, anti-DNA antibodies, rheumatoid factor and antiphospholipid antibodies was negative. However, xANCA were detected at a high titre of 1 : 160. The IgA serum level was elevated at 4·46 g L^{-1} (normal $< 2{\cdot}96$). Light microscopy of a skin biopsy showed leucocytoclastic vasculitis with swelling of endothelial cells, fibrin deposits in the vessel walls, a perivascular cellular infiltrate rich in neutrophils with nuclear dust, and extravasated erythrocytes. Direct immunofluorescence microscopy of an early lesion disclosed deposits of IgA and C3 in the dermal vessel walls.

Treatment with losartan, mianserin and acetylsalicylic acid was discontinued, with a rapid improvement of the skin lesions within 3 weeks. Thereafter, mianserin and acetylsalicylic acid were reintroduced without side-effects. Eighteen months after discontinuation of losartan, xANCA were detected at a titre of 1 : 1280.

SHP is a systemic small-vessel vasculitis frequently associated with an elevated serum level of IgA1. It predominantly affects the skin, joints, gastrointestinal tract and kidneys.[1] While the prognosis is usually excellent, progressive renal disease occurs in approximately 5% of patients.[1]

In our patient, the development of SHP appeared to be triggered by losartan, which was assessed as a probable (61–80%) cause according to the World Health Organization causality categories.[4] This idea was supported by the observation that the cutaneous lesions developed within 4 weeks after introduction of losartan and by their self-limited course once the drug was discontinued. Another case of SHP related to losartan has been reported, in which there was recurrence upon re-exposure to the drug.[2] One case of SHP related to acetylsalicylic acid has been reported, although chronic SHP has been successfully treated with acetylsalicylic acid.[5] While mianserin and acetylsalicylic acid were reintroduced without relapse, re-exposure to losartan was not attempted for ethical reasons.

Our case was unusual for the presence of xANCA. ANCA-associated small-vessel necrotizing vasculitis, such as in Wegener's granulomatosis, Churg–Strauss syndrome or microscopic polyangiitis, may present with the same clinical and histological features as SHP. In these conditions, antigen specificity of ANCA characteristically includes either anti-proteinase 3 or antimyeloperoxidase (MPO-ANCA) antibodies, which are thought to induce vascular injury by activating circulating neutrophils and monocytes.[1] In contrast, xANCA are a specific and sensitive marker for ulcerative colitis and primary sclerosing cholangitis, and are rarely found in Crohn's disease and other types of colitis.[6] Interestingly, various drugs have been reported to cause vasculitis in association with the presence of MPO-ANCA, such as propylthiouracil, hydralazine, penicillamine, allopurinol and sulphasalazine.[7] In our patient, who had no evidence of a gastrointestinal disorder, the role of xANCA in development of vasculitis and their relation with losartan intake appears unlikely. In fact, xANCA persisted at high titre despite complete resolution of the skin disease and discontinuation of losartan.

Angiotensin-converting enzyme inhibitors represent one of the most effective classes of antihypertensive agents in patients with IgA or SHP glomerulonephritis.[8] They reduce levels of angiotensin II, a potent vasoconstrictor of small vessels, and increase bradykinin levels. Our observation raises the hypothesis that the disturbance of angiotensin II pathways resulting from losartan intake has a deleterious effect on endothelial cells, and thereby induces a small-vessel vasculitis.

Together, our case and the previous case suggest that leucocytoclastic vasculitis may represent a potential side-effect of losartan. Knowledge of this cutaneous complication is important in view of the increasing prescription of this novel class of antihypertensive agent.

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Chronic glomerulonephritis remarkably improved after surgery for acne conglobata of the buttocks

Sir, Acne conglobata is a chronic inflammatory disease with multiple comedones, pustules, abscesses and scars commonly affecting the trunk and buttocks. Local hyperhidrosis, poor personal hygiene or mechanical factors may contribute to the buttock lesions; however, although immunological disorders[1] or hormonal abnormalities[2] have been suggested to be important in this disorder, its precise pathogenesis is still unknown. Some reports have described acute glomerulonephritis or renal amyloidosis associated with acne conglobata.[3–5] In these cases, the renal diseases were irreversible and progressive despite successful treatment of the cutaneous lesions. We present a patient with chronic glomerulonephritis associated with severe acne conglobata of the buttocks, in whom the renal disease remarkably improved after radical surgical treatment of the cutaneous disease.

A 47-year-old Japanese man had suffered from multiple folliculitis-like eruptions on his buttocks, trunk and nape of the neck for about 30 years. Although various conservative therapies had been used, the abscesses on the buttocks had gradually aggregated and grown to form ugly scarring plaques and nodules with draining fistulae (Fig. 1). Microscopic haematuria and proteinuria were detected at the age of 43 years. Blood analysis showed severe iron-deficiency anaemia (haemoglobin $6{\cdot}5\ g\ dL^{-1}$), white cell count $13{\cdot}6 \times 10^9\ L^{-1}$ with 82% neutrophils, and erythrocyte sedimentation rate 91 mm in the first hour. Total protein, serum albumin and γ-globulin levels were 8·9, 2·6 and $4{\cdot}4\ g\ dL^{-1}$, respectively. Serum M-component was absent. Immunological studies showed high levels of IgG, IgA, C3d-binding and C1q-binding immune complexes. No other immunological abnormalities were found. Blood sugar estimation showed prediabetes. The serum creatinine level

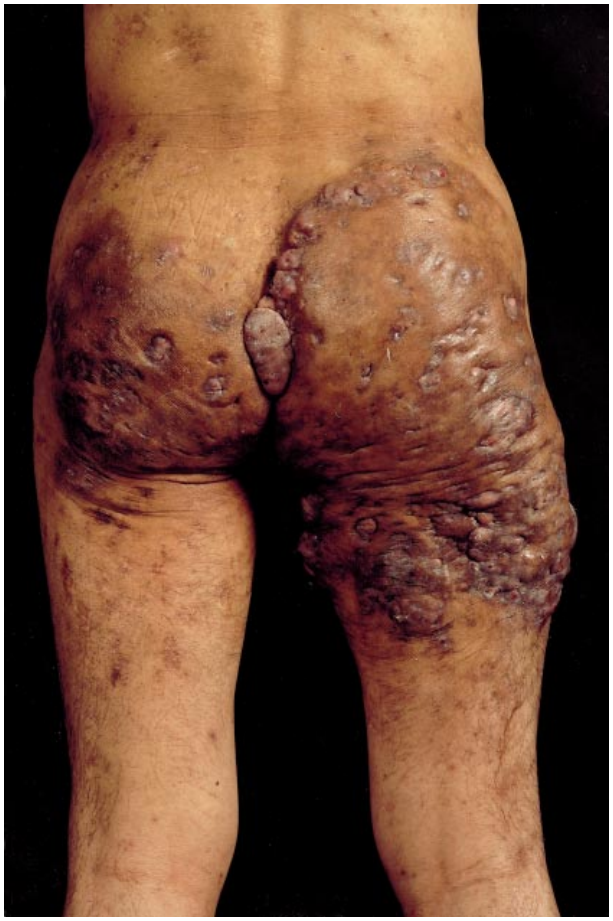

Figure 1. Clinical appearance of acne conglobata of the buttocks.

was $1{\cdot}3\ mg\ dL^{-1}$. Urinalysis showed a high level of occult blood and mild proteinuria of $1{\cdot}18\ g\ day^{-1}$. Renal biopsy showed mesangial proliferative progressive glomerulonephritis without amyloid deposition. Approximately 40% of glomeruli showed sclerotic change. There was no evidence of internal or cutaneous malignancy.

The lesions of the buttocks, perianal area and right posterior thigh were resected including the affected subcutaneous fat tissue and were left open to heal by granulation initially. A week later, good granulation tissue had developed, and split-thickness skin obtained from the back was meshed to a threefold broader dimension and grafted on to the defects. After the removal of the skin lesions, haematuria and proteinuria gradually improved and finally the urinalysis became normal. White cell count and γ-globulin level subsided and the anaemia showed recovery. One year after the operation, the grafted areas remained in good condition without recurrence. Urinary occult blood was still negative and urinary protein levels were within normal limits.

In this case, surgical excision of the purulent skin lesions definitely resulted in the reduction of haematuria and proteinuria. The precise reason is not apparent at this time. Chronic antigenic stimulation by bacteria from the infectious cutaneous lesions may have induced the high level of

γ-globulin and promoted the circulating immune complex formation, leading to deposition of formed immune complexes in the glomeruli, which may be one of the causative or enhancing factors of glomerulonephritis. Other factors, such as cytokines or endotoxins released from skin lesions, may also participate. We speculate that removal of the cutaneous lesions led to cessation of antigenic stimulation and decreased production of other involved factors, and therefore rescued some of the involved glomeruli. However, some severely damaged glomeruli did not recover. Further studies and long-term follow-up are required to clarify this correlation between skin and renal lesions.

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Dystrophic calcinosis cutis in venous ulcers: a cause of treatment failure

SIR, An 83-year-old woman had an 8-month history of painless ulceration on the lateral aspect of the left leg, which had been unresponsive to treatment with regular dressings. She had a past medical history of bilateral sclerotherapy for varicose veins in 1969, hypertension, type 2 diabetes, and carcinoma of the left breast in 1994 treated by mastectomy and axillary node clearance, with no evidence of recurrence. Medication comprised tamoxifen, metformin, nifedipine and indomethacin.

Examination revealed an area of ulceration on the outer aspect of the lower left leg measuring 8 × 5 cm. There was chalky material extruding from the wound (Fig. 1a). Clinically she had bilateral chronic venous insufficiency with varicose veins. X-ray confirmed the presence of extensive subcutaneous calcification in both legs (Fig. 1b). Investigations including full blood count, erythrocyte sedimentation rate, C-reactive protein, urea and electrolytes, liver function tests, thyroid function, calcium, phosphate and parathyroid hormone were all normal. The ankle/brachial pressure index was > 0·8 in both legs. She was treated on an outpatient basis with four-layer compression bandaging, but 6 months later her ulcer had failed to heal and continued to express chalky material.

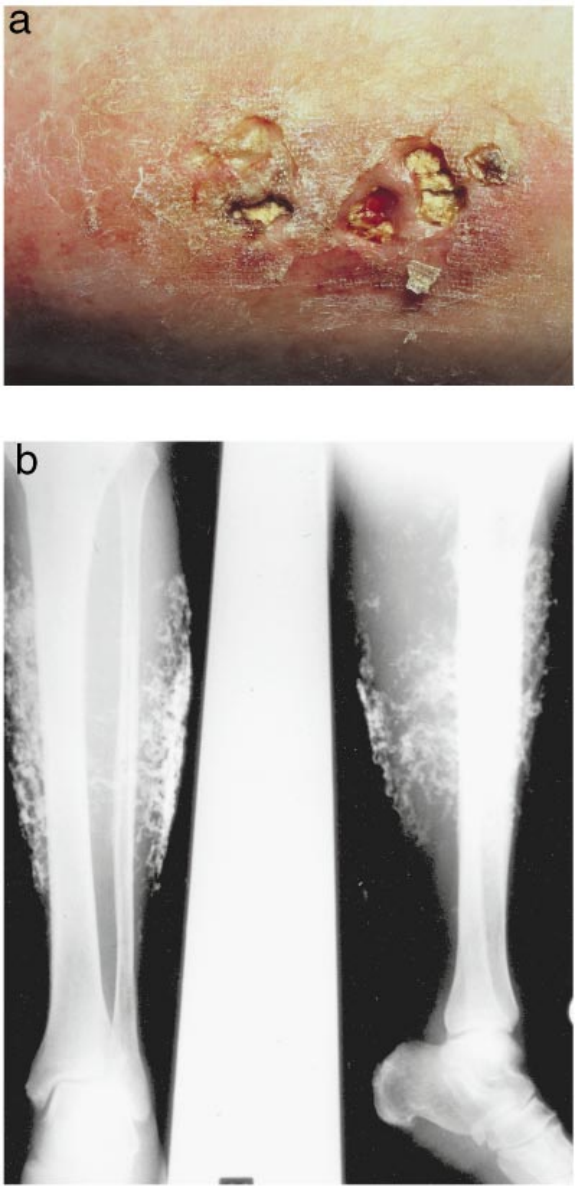

Figure 1. (a) Leg ulceration with visible extrusion of calcium. (b) X-ray of left leg showing extensive subcutaneous calcification.

Calcinosis cutis (CC) is the abnormal deposition of calcium and phosphate in the skin, and can be subdivided into four categories: dystrophic, metastatic, idiopathic and iatrogenic.[1] Dystrophic CC follows localized or widespread tissue damage to connective or adipose tissue. Calcification is confined to the dermis. Serum concentrations of calcium, phosphate and their regulatory hormones are always normal. Localized dystrophic CC can follow trauma, infections, surgery or acne, and can be associated with a variety of benign cutaneous neoplasms. It can also be seen in patients with venous

stasis and varicose veins. In this situation, venography demonstrated that the calcification did not involve vessels.[2] Presumably inflammation resulting from venous leakage into adjacent tissue led to calcification. Widespread tissue damage and dystrophic calcification can occasionally be seen in a variety of connective tissue disorders including dermatomyositis and scleroderma.

By contrast, in metastatic CC there is an underlying abnormality of calcium and/or phosphate metabolism, leading to either hypercalcaemia or hyperphosphataemia. This typically results in calcification of blood vessels, muscle and internal organs, but may also involve the skin. The tissues in which calcium is deposited are normal. Metastatic CC is most frequently seen in chronic renal failure where the cutaneous manifestations vary from benign nodular calcification to calciphylaxis, with necrosis of skin and a high mortality rate.

Mitochondria can concentrate both calcium and phosphate to levels exceeding their solubility product and act as the nidus for calcium deposition in both dystrophic and metastatic CC. In dystrophic CC, high intracellular calcium levels follow cell membrane damage.

Idiopathic CC occurs in the absence of tissue damage or demonstrable abnormalities of calcium and phosphate metabolism. Iatrogenic CC is occasionally seen as a complication of extravasation of intravenous calcium. There is likely to be a combination of locally high levels of calcium combined with tissue damage.

Venous disease is the commonest cause of leg ulceration. Subcutaneous calcification has been found in 10% of patients with chronic venous insufficiency but is rarely reported. It almost exclusively affects postmenopausal women.[2] Ninety per cent of patients with dystrophic CC complicating venous leg ulceration have non-healing or recurrent ulcers.[2] Aggressive surgical management, including extensive debridement and skin grafting, may be the most effective treatment.[3,4]

Physicians should be aware that dystrophic CC complicating venous leg ulceration is a potential reason why leg ulcers may fail to respond to conservative management. X-ray assessment and surgical referral may be appropriate in some cases.

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Angiolymphoid hyperplasia with eosinophilia in the oral mucosa

Sir, Angiolymphoid hyperplasia with eosinophilia (ALHE) is a rare benign disorder affecting mainly the head and neck with multiple nodules.[1] Lesions of the oral mucosa are extremely rare.[2–6] Similarites exist between ALHE and Kimura's disease, including the pathological findings of a proliferation of both lymphoid and angiomatous tissues accompanied by eosiniphils,[7] such that ALHE has been confused with Kimura's disease.[8] However, vascular structures lined with endothelial cells having large, round, and occasionally indented nuclei protruding into the lumina are the main histological findings in ALHE, but are not prominent in Kimura's disease. Consequently, ALHE and Kimura's disease are thought to be two different entities.[9] We present a rare case of angioloymphoid hyperplasia with eosinophilia affecting the oral mucosa of a 60-year-old Japanese male, presenting as nodules of the buccal mucosa and swelling of the gingivae.

The patient, an otherwise healthy 60-year-old Japanese male, first noticed a swelling of his tonsil, then discovered a small nodule on the mucous membrane of his left lower buccal mucosa and swelling of his gingivae. Because the nodules increased in number and size for 4 months, he was hospitalized for further investigation and treatment. An elliptical, dome-shaped mass, measuring about 1×2 cm in diameter was observed in the left buccal mucosa. The nodule was elastic firm, and covered by normally textured mucous membrane (Fig. 1a). A 7-mm diameter nodule in the right side of the buccal mucosa was also observed. The upper and lower gingiva was swollen, and swelling of the tonsil and regional lympahadenopathy were noted. The patient had a history of herpes simplex. Laboratory tests showed eosinophilia ($1008\ mm^{-3}$, 14% of white blood cells) and a high serum IgE level ($989\ U\ mL^{-1}$). Anti-*Candida albicans* IgE antibody was not present. Histological examination of the buccal biopsy specimens revealed an increase of many small vessels. The vascular walls consisted of prominent endothelial cells with histiocytoid appearance, which protruded into the lumen. Many eosinophils and lymphocytes were also seen around the vessels (Fig. 1b). Lymphoid follicle formation was also observed in the left buccal biopsy. The germinal centres were mainly positive for CD20 and the perifollicular areas were positive for CD4 and CD8 with predominance of CD4. IgE deposition was observed in the germinal centres. The histological findings of the gingiva were similar. A diagnosis of ALHE was made on the basis of the typical histological features. Oral prednisolone, 10 mg daily, reduced the lesions after one month's treatment. The eosinophilia and serum IgE level also improved.

In 1969, Wells and Whimster published the first report in English that described nine cases of ALHE characterized by a marked vascular proliferation with infiltration of eosinophils, which they termed subcutaneous angiolymphoid hyperplasia

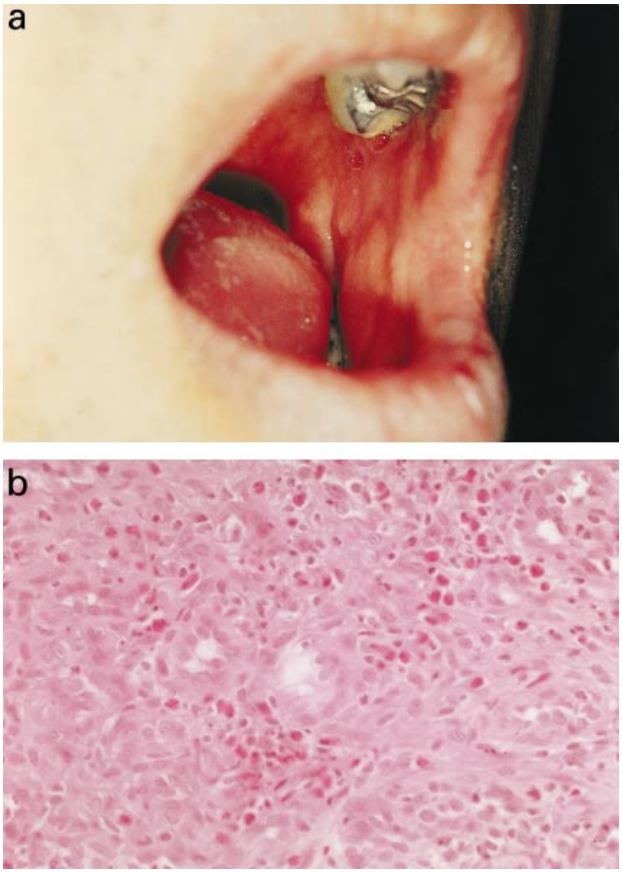

Figure 1. (a) An elliptical, dome-shaped mass, measuring about 1 × 2 cm in diameter covered by normally textured mucous membrane of the left buccal mucosa. (b) Proliferation of irregular-shaped blood vessels with numerous eosinophils is seen. The vascular walls contain prominent endothelial cells, which protruded into the lumen (original magnification × 200).

with eosinophilia.[1] In our patient, the longer duration left buccal nodule had an increase of the number of small vessels and lymphoid follicle formation with infiltration of eosinophils. The histological findings of the more recent right buccal mucosa and gingiva showed aggregations of small vessels, whose vascular walls consisted of prominent endothelial cells with the infiltration of eosinophils. The main histological finding of this case is vascular aggregates with large endothelial cells, resembling newly formed blood vessels. This suggests that the histology of ALHE is a spectrum which ranges from a vascular predominance in early active lesions to a predominance of inflammatory cells in later stages, the latter involving formation of lymph follicles.

There have been 25 cases of oral ALHE described in the literature so far.[2–6] Clinically, oral ALHE appears as a solitary asymptomatic nodule, yet macules, plaques, ulcers or even tumours have been described. The lip is the most frequent site, followed by the buccal mucosa, palate and tongue; swelling of the gingiva has not been frequently described. Our patient displayed both nodules of buccal mucosa and swelling of the gingivae.

There are many hypotheses that may explain these differences including infection, allergy, trauma, an overgrowth of an atypical population of endothelial cells and inflammatory skin manifestation. A recent report indicated that the serum IL-5 level was correlated with the state of disease in ALHE.[10] It is considered probably to be of allergic origin and may be an immunological disturbance. IgE deposits were observed in the centre of the lymphoid follicles and tissues. Furthermore, peripheral eosinophilia in our patient also suggests that an immunological disturbance may be regarded as important in the aetiology of ALHE.

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Intraosseous epidermoid cyst mimicking psoriasis

SIR, We describe a patient with an intraosseous epidermoid cyst of her left little finger, which clinically mimicked psoriasis and radiologically raised concerns as regards a malignant bone tumour.

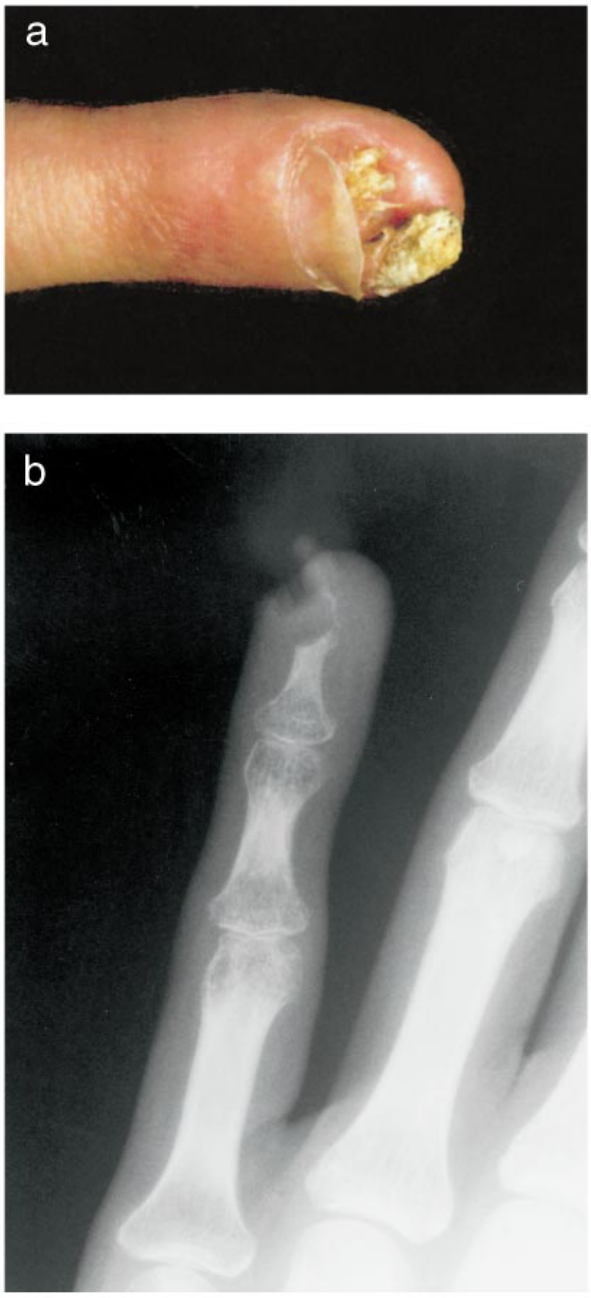

Figure 1. (a) The distal left little finger was swollen and erythematous, with a warty lesion raising up a shortened nail plate. (b) An X-ray suggested a malignant osteolytic tumour.

A 24-year-old woman presented with a 7-month history of a warty lesion on the tip of her left little finger (non-dominant hand). An initial red swelling of the end of the digit was followed by a warty lesion that had started to lift the nail up, but was causing only minimal discomfort. A diagnosis of a common wart was made by her general practitioner, and treated with liquid nitrogen cryotherapy. On review a few weeks later, the warty lesion had increased in size with more erythema and swelling of the terminal digit, which had become more painful and with some limitation of movement. The patient was referred to the dermatology department. She had had two epidermoid cysts excised from her scalp previously. There was no other medical history of note and she was not taking any systemic medication. She gave a history of her mother and maternal aunt having psoriasis.

Examination revealed a swollen and erythematous distal left little finger with a warty lesion raising up a shortened nail plate (Fig. 1a). There was no evidence of psoriasis elsewhere and she had an epidermoid cyst on her scalp. In view of the anatomical site, the clinical features and the family history, psoriasis was considered as the most likely diagnosis.

An X-ray of the digit (requested in view of the considerable discomfort and to rule out the possibility of subungual exostosis) raised concerns as regards a malignant osteolytic tumour (Fig. 1b). The lesion was excised; histology was consistent with a keratinizing epidermoid cyst with no evidence of neoplasia. A year after surgery, the digit appeared clinically clear with minimal erythema only.

Intraosseous epidermoid cysts arise most frequently in the skull and distal phalanges of the hand.[1] It is believed that lesions in the phalanges could be due to trauma leading to the introduction of epidermis into bone or a bony erosion caused by an enlarging cyst in a small non-expansile compartment.[2] Intraosseous epidermoid cysts of the fingers seem to be more common in men, and the left hand has a higher reported incidence of cysts than the right.[3] The most common symptom is swelling of the finger tip associated with redness, pain and tenderness.[2] X-ray findings are characteristic but not diagnostic and show a well-defined osteolytic lesion outlined by a thin rim of sclerotic bone.[1–5]

Magnetic resonance imaging was recently used to demonstrate a giant epidermoid cyst,[6] and ultrasound imaging is a cheap and readily available alternative for demonstrating epidermoid cysts.[7] Conservative treatment is recommended.[1–5] Amputation should not be performed; curettage or surgical excision is preferred.[8]

Our patient presented with clinical features mimicking psoriasis of the digit but radiography and histology were consistent with an intraosseous epidermoid cyst. We are aware of a case report of intraosseous epidermoid cyst in a metacarpal mimicking malignancy,[9] similar to our patient. Without the X-ray of the digit, psoriasis would have been the clinical diagnosis in view of the clinical picture as well as the positive family history of psoriasis. It is also of interest that our patient with an intraosseous epidermoid cyst of her finger also had epidermoid cysts on her scalp; we are not aware of any reported similar association.

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Dose thresholds and local anhidrotic effect of botulinum A toxin injections (Dysport®)

SIR, We read with interest the article from Braune *et al.*[1] analysing dose dependency and duration of botulinum toxin type A (BTX-A)-induced suppression of the sweat gland activity in healthy volunteers. For the first time threshold doses for the suppression of sweating have been defined using iodine starch staining and the quantitative sudomotor axon reflex test (QSART). Iodine starch staining indicated a threshold dose of 10 mU Dysport® ($2{\cdot}5\ cm^{-2}$) leading to a visible anhidrotic skin spot at the lateral aspects of the lower leg, after three weeks in all subjects. We would like to add the following comments to this article.

We have observed in clinical practice that size of the anhidrotic area after BTX-A injection is dependent on the severity of sweating. In normal volunteers fewer BTX-A injections are necessary to achieve confluent anhidrosis of one palm, whereas patients with severe palmar hyperhidrosis need more injection sites to reach a satisfactory effect.[2–5]

Secondly, the size of the anhidrotic area is dependent on the spread of the BTX-A solution and on the local number of sweat glands of a specific skin area. Bushara[2] obtained a circular area of complete anhidrosis of 5–6 cm diameter for 11 months after performing a single subcutaneous injection of 20 mU BTX-A (Dysport®) in the dorsum of the hand, whereas circular anhidrotic areas with a diameter of 3–4 cm after injecting 20 mU BTX-A (Dysport®) at six sites in the palm were documented in healthy volunteers.[3]

As stated in the manufacturers' recommendations, Dysport® can be diluted with 1 mL, 1·5 mL, 2 mL or 2·5 mL of saline diluent. Currently, two preparations of BTX-A are available, Dysport® (Ipsen Pharma) and Botox® (Allergan Inc.). One formulation appears to be more active in saline, perhaps because of different stability.[6] The authors used different BTX-A doses in the same volume of diluent (1 mL saline), diluting the vial of Dysport® with a volume ranging from 4·2 mL to 200 mL. Clinical studies reported effective doses to range between 200 mU and 250 mU Dysport® per side (one vial diluted with 1·5 or 2 mL) in axillary and palmar hyperhidrosis.[5,7] Recent studies show that the biological availability of Dysport® can be enhanced by supplementing with albumin, lowering its concentration and increasing the injection volume.[8,9] Therefore, the suppression of sweating after injection of BTX-A (Dysport®) diluted in high volumes of saline should be interpreted with caution.

In conclusion, the threshold doses of BTX-A for the treatment of hyperhidrosis depend on the severity of the condition and the location of sweating. Furthermore the diluent and dilution can also affect potency of BTX-A. These factors should be considered when using BTX-A injections in clinical practice.

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Xanthogranuloma is the archetype of non-Langerhans cell histiocytoses

SIR, We read with great interest the recent editorial about 'The confusing state of the histiocytoses' by Dr Chu.[1] We feel that several points arising from this editorial require a comment and further elucidation.

For some years now it has been recognized that the application and use of the term 'histiocytoses' is indeed confusing. Historically, the term was first introduced by Kiyono and then made popular in the early 1930s by Aschoff who regarded histiocytes as part of the reticuloendothelial system.[2] These cells, capable of phagocytosis and ameboid movement, were wrongly thought to derive from locoregionary connective tissue, hence the term 'histiocyte' (from the Greek 'ιστον, meaning tissue). However, there are many more 'histiocytes', such as mast cells, fibrocytes, muscle cells, nerve cells and endothelial cells, and one could almost equally speak of 'somatocytes'. Later, van Furth *et al.*[3] recognized that this is a much more dynamic system. Macrophages derive from stem cells in the bone marrow, circulate through the organism as monocytes via blood, leave the blood system into the various tissues for phagocytosis, or alternatively stay there for some time, and then finally die; other variants such as Langerhans cells[4] home into the epidermis or other epithelia, digest and process antigens, leave the skin, and migrate via lymphatics to the T-cell dependent zones of lymph nodes. While there is continuous recruitment of all types of macrophages from the bone marrow, those cells having performed their function die: this can be seen in tuberculoid or palisading granulomas of conditions such as tuberculosis, granuloma annulare, necrobiosis lipoidica or necrobiotic xanthogranuloma. Some of these cells may derive from locally resting tissue macrophages in the sense of 'histiocytes' as originally defined;[2] most macrophages are derived from the circulation. The term 'histiocyte' does not clarify if macrophages were already in the tissue before tissue damage or were recruited from the blood afterwards. In our view 'dermal dendrocytes'[5] are just another evasion of this question, which cannot be answered by pure morphological criteria. A wide variety of cells, and not only 'precursors of macrophages',[5] may have dendritic morphology, including Langerhans cells, melanocytes, fibrocytes and endothelial cells. Their heterogeneity has been outlined by immunohistochemistry which shows a factor XIIIa-positive variant in the papillary dermis, but a CD34-positive variant in the reticular dermis. Moreover, both of these cell types are by no means restricted to the dermis, but may be seen as factor XIIIa-positive macrophages in the lung for the former, or CD34-positive dendrocytes in perivascular subcutaneous tissue for the latter, respectively.

We feel that it is more logical to avoid these flawed concepts of histiocytoses and dermal dendrocytes but instead, where possible, to use terminology according to the actual differentiation of these disorders. Basically, the Histiocyte Society has subdivided histiocytoses into three classes: class 1, Langerhans cell histiocytoses; class 2, non-Langerhans cell histiocytoses; and class 3, malignant histiocytoses, which mostly consist of large cell anaplastic lymphomas. Similar to Lichtenstein who in 1953 first recognized that Abt-Letterer-Siwe disease, Hand-Schüller-Christian disease and eosinophilic granuloma (of the bone) are just variations of one disease,[6] Chu[1] tries to bring some order to class 2 by relating the histopathological appearance of these entities to a time cycle of clinicopathological events. We congratulate him on this endeavour, agree that the macrophage is the essential contributor to this process, and wish to draw attention to our article published in the *American Journal of Dermatopathology* some years ago.[7] Based on an experience of then 150, now more than 300, cases of non-Langerhans cell histiocytoses we demonstrated and now reiterate that xanthogranulomas are the archetype of this process characterized by a variable mixture of basically five morphological types of macrophages (Fig. 1): vacuolated, with a slightly vacuolized cytoplasm; xanthomatized, with prominent xanthomatization of a largely expanded cytoplasm; scalloped, with bizarre stellate macrophages with spidery cell extensions; oncocytic, with a finely granular, homogeneously eosinophilic cytoplasm (from the Greek ονκειν for swollen, synonymously known as ground glass appearance in giant cells); and spindle-shaped, with oval nuclei and long slender bipolar cell extensions. We showed that all of these cell types can be found to a variable degree in juvenile and adult xanthogranulomas.[7]

Besides a polymorphous mixture of these cell types in xanthogranulomas, some lesions show a mostly monomorphous appearance of one cell type (Fig. 1). When vacuolated macrophages are predominant, solitary lesions are

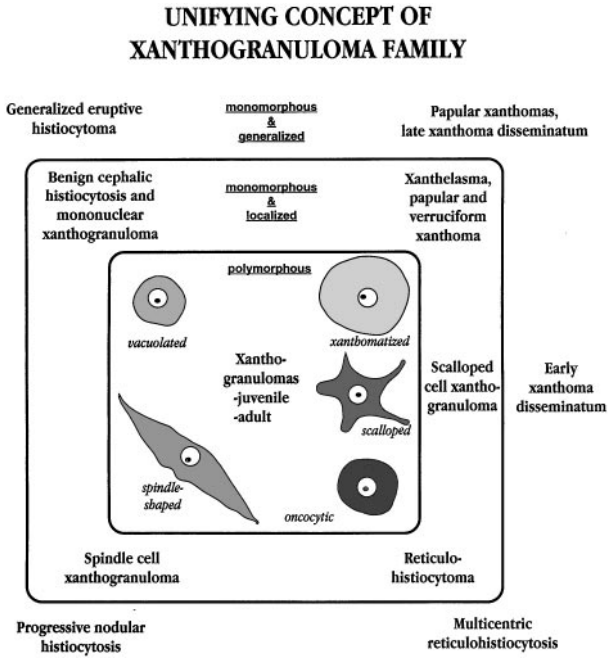

Figure 1. Unifying concept of xanthogranuloma family. This figure is a slightly modified version of a schematic drawing originally published as Figure 12 in the review article by Zelger *et al.*[7] and is reproduced with the permission of the publisher, Lippincott Williams & Wilkins, Inc.

known as the mononuclear variant of xanthogranuloma, several to multiple papules to nodules mostly localized to the head and neck as benign cephalic histiocytosis, and myriads of generalized papules on the face, trunk and extremities are termed generalized eruptive histiocytomas. When xanthomatized macrophages are dominant, plaques around the eyes are known as xanthelasma, the most common non-Langerhans cell disease (in contrast to hyperlipidaemia-associated xanthomas which have increased serum levels of lipids, are quickly reversible and show extracellular lipids), a plaque mostly on mucous membranes is a verruciform xanthoma, and a single exophytic papule to nodule elsewhere is known as papular xanthoma. The same lesions if generalized are known as (multiple) papular xanthomas and fully developed stages of xanthoma disseminatum. When scalloped cells are dominant, a single lesion is known as scalloped cell xanthogranuloma, and the generalized variant as an early manifestation of xanthoma disseminatum. Predominance of oncocytic macrophages in a solitary lesion is called reticulohistiocytoma or reticulohistiocytic granuloma, while this process when generalized is termed multicentric reticulohistiocytosis. Finally, predominance of spindle-shaped macrophages in a single lesion has been described as spindle cell xanthogranuloma, and generalized papules, nodules to tumours as progressive nodular histiocytosis. Numerous cases which show one type of lesion beside another, and cases following a time cycle with variable patterns, are in accordance with these observations and concepts.[7] The editorial by Chu,[1] as well as two publications on progressive nodular histiocytosis in the same issue of the *British Journal of Dermatology*,[8,9] reinforce these observations. Similar to Lichtenstein,[6] and subsequently the Histiocyte Society,[10] who revolutionized a confusing potpourri of entities under the heading of a Langerhans cell disease, we agree that at present Dr Chu is right in lumping together all the entities as listed above. The basic pathological progress of all these lesions is a nodular to diffuse dermatitis but with predominance of macrophages, termed xanthogranuloma, the archetype of all these disorders; the other entities are just variations on the theme.

Similar to Langerhans cell histiocytosis, it is important to note that diagnosis neither predicts prognosis nor determines therapy. While diseases in childhood are mostly widespread, their prognosis is excellent with nearly all lesions melting away within several months to a few years. Usually no underlying disorder is detected in these cases. Aggressive treatment in these cases as suggested by Chu[1] might prove to be successful, yet in reality only mirrors the natural course of disease. In view of the possible short- and long-term side-effects of radiotherapy and chemotherapy, such an approach seems unjustified. In contrast, adult variants are frequently solitary lesions often cured by excision; generalized lesions are rare in adulthood, but when they occur they may be resistant to every therapy, rarely regress, and not uncommonly show some underlying disorder such as lupus erythematosus, dermatomyositis, Hashimoto thyroiditis or various neoplasias, lymphomas or leukaemias. Therapy of the underlying process occasionally parallels a wax and wane of histiocytic lesions.[11]

We agree that, for the majority, aggressive therapy for xanthogranulomas other than for an associated underlying malignancy does not seem to be justified. Interestingly, some therapeutic benefit may arise from immunomodulation by interferons, as recently described.[12] In future we hope that xanthogranulomas and their variants of non-Langerhans cell histiocytoses may well be more treatable.

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Xanthogranuloma is the archetype of non-Langerhans cell histiocytoses: reply from author

Sir, I would agree with Drs Zelger and Cerio that the term histiocytosis is confusing, but I feel that a change in

terminology would further confuse the issue. It is not only the dermatologist that sees patients with histiocytoses; patients are seen by paediatricians, oncologists and haematologists and the terminology adopted by the Histiocyte Society[1] has been broadly accepted. The classification of the Histiocyte Society has helped to reduce confusion about the histiocytoses in classifying all Langerhans cell disease as Class I histiocytosis and malignancies of the histiocyte as Class III histiocytosis. The major confusion comes with the Class II histiocytoses, which are a hotchpotch of disparate conditions, unified by being nonmalignant diseases derived from cells of the monocyte/macrophage/dendritic cell origin.

I would certainly agree with Drs Zelger and Cerio that the xanthogranulomatous conditions are an important subset of the Class II histiocytosis but not all Class II histiocytoses are xanthogranulomatous. The viral-associated and familial haemophagocytic hymphohistiocytosis, mulicentric reticulohistiocytosis, Rosai Dorfmann disease, and sea-blue histiocytosis all appear to have different pathophysiological mechanisms and the lesional cells are not derived from factor XIIIa positive histiocytes.

I would disagree with Drs Zelger and Cerio as far as therapy is concerned. Obviously, in juvenile xanthogranuloma the prognosis is excellent and no treatment is usually needed. This is not necessarily the case in xanthoma disseminatum or in generalized eruptive histiocytosis and in progressive nodular histiocytosis, the disease is progressive causing severe morbidity. These latter diseases can cause significant reduction of the quality of life of patients and in such cases I would encourage early aggressive treatment to try to modify the disease at a time when it is potentially responsive to treatment.

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Book Reviews

Pathology of Infectious Diseases. Vol 1. Helminthiases (2000). Edited by W.M.Meyers, R.C.Neafie, A.M.Marty, D.J.Wear. Washington: Armed Forces Institute of Pathology. ISBN 1-881041-65-4. Price $145.

As the title suggests, this book is really aimed at pathologists, and is of primary interest to those working in the tropics or in tropical disease hospitals. Its relevance to the average dermatology department in the U.K. would be purely for occasional reference, or when microscopy turns up some unexpected apparent parasite (there are a series of fascinating pictures of things that mimic helminths in tissues, including starch in the lungs and a feather in a child's nose). Most chapters cover specific infections and therefore require reasonable suspicion of a diagnosis from the outset. With the exception of the introductory chapter, where the first text citation to a figure occurs several pages after the figures, the overall layout is consistent and well planned.

The advertising flyer for this book states that it is drawn from the greatest repository of human pathological material in the world, and that it includes superb photographs. I cannot vouch for the former part of this statement, but the latter is undoubtedly true. The few clinical pictures, presumably often taken under less than optimum circumstances, are of patchy quality but the photomicrographs, which constitute the majority of the illustrations, are almost universally excellent. While this book is not aimed at dermatologists, it can still be commended on its comprehensive and well-illustrated pathology.

Neil H.Cox

Dermatology Nursing: A Practical Guide (2000). Edited by E.Hughes, J.van Onselen. London: Churchill Livingstone. ISBN 0443062099. 286 pp., hardback. Price £32.95.

This is an excellent book, well put together and set out in an easy-to-read format. The headings are distinctive and I liked the inclusion of boxes to contain specific facts. The signpost boxes are a particularly good feature. It is also a good point that the key facts are listed. The knowledge contained appears both topical and up-to-date. All chapters are well referenced and well sourced. A well-rounded textbook, which will be of benefit both for those with a rudimentary knowledge of dermatology nursing and for specialist dermatology nurses who will find this an invaluable tool to use as a source of quick reference and a starting point, with the aid of included references, to gain a more in-depth insight into a specific condition. Definitely a must for all dermatology units and interested primary care nurses.

Julie Bowman

Allergic Contact Dermatitis – Chemical and Metabolic Mechanisms (2000). C.K.Smith, S.A.M.Hotchkiss. Taylor & Francis. ISBN 0415250471. 344 pp., hardback. Price: £70.00

Why are some substances (xenobiotics) allergenic whereas other are inert or irritants? If you read this book you will know the answer. It is well written in a clear manner that a non-boffin such as myself can understand. The diagrams and chemical formulae are plentiful and also easily understood.

I have two quibbles with the contents. Firstly, the authors have not attempted to address type 1, 2 or 3 hypersensitivity reactions in relation to skin; probably very wise as it would be at least another book in its own right. Secondly, there is very little about two relatively new concepts, 'danger irritant signals' and dose per unit area, both being important factors in the pathogenesis of allergic contact dermatitis (ACD). However, as it states on the back cover 'the book is the most comprehensive analysis of the biochemistry of ACD currently available, this is an essential reference for biochemists, toxicologists, pharmacologists, be they from academia, the government laboratory or from the food, cosmetic and pharmaceutical industries'. I would add also the enquiring patch tester as well.

JOHN ENGLISH

News and Notices

Course on Infectious Diseases
25–27 October 2001, Liverpool, U.K.

This is a residential course, aimed at experienced and newly appointed consultants in dermatology, with the focus on infectious diseases. The course will include imported and tropical dermatology, HIV infections and new developments in therapy. For further details, please contact: Jeane Adly, Department of Medical Mycology, St Thomas' Hospital, London, U.K. Tel.: + 44 20 7925 9292 ext. 1374; fax: + 20 7922 8227; e-mail: jeaneadly@yahoo.com

Paediatric Dermatology Course
1–2 November 2001, Liverpool, U.K.

This clinical course is held annually in Liverpool and is aimed at Specialist Registrars and recently appointed Consultant Dermatologists and Paediatricians. An important component of the course is small-group clinical teaching. Numbers are limited to 12. For further details contact: Dr. G.Sharpe, Course Organiser, University of Liverpool, Dermatology Unit, Department of Medicine, UCD Building, Liverpool L69 3GA, U.K. Tel.: + 44 151 706 4030; fax: + 44 151 706 5842; e-mail: grs@liverpool.ac.uk

Clinicopathological Workshop on Skin Diseases (Cutaneous Lymphoid Infiltrate)
2 November 2001, London, U.K.

This course is the seventh in a rolling programme of eight dermatopathology workshops, combining slide, self-assessment, lectures and discussion groups. It is suitable for SpRs in pathology and dermatology. Places are limited, so reservation is essential. Course fee is £60 including coffee, lunch and tea (North Thames SpRs no charge). For further details contact: Dr. Rino Cerio, Department of Morbid Anatomy, Institute of Pathology, Royal London Hospital, Whitechapel, London, U.K. Tel.: + 44 20 7377 7348; fax: + 44 20 7377 0949; e-mail: l.singer@mds.qmw.ac.uk

British Society of Paediatric Dermatology 16th Annual Meeting
9–10 November 2001, Cambridge, UK

The programme includes invited speakers, free communications and clinical cases. Abstracts for free communication/ registration should be received by 29 September 2001. For further details, including abstracts and registration forms, please contact: Mrs Julie Graham, Postgraduate Medical Centre, Clinical School, Box 111, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2SP. U.K. Tel: + 44 1223 274419; fax: + 44 1223 217237; e-mail: ag230@medschi.cam.ac.uk

The Sixth Asian Dermatological Congress
11–13 November 2001, Queen Sirikit National Convention Centre, Bangkok, Thailand

For further information, contact: The Secretary General, c/o Organizing Committee, Institute of Dermatology, 420/7 Rajavithi Road, Rajathevi, Bankgkok 10400, Thailand. Fax: + 662 246 8894; website: www.thaiderm.org/adc

The Thirteenth International Symposium in Contact Dermatitis and the First Latin American Symposium in Cutaneous Allergy
23–25 November 2001, Montevideo, Uruguay

The event is being organised by the International Contact Dermatitis Research Group (ICDRG) and the South American Contact Dermatitis Research Group (DERMOSUR). Contact: Dr. Iris Ale, Organizing Committee, Arazati 1194, 11300 Montevideo, Uruguay. Fax: + 5982 622 0882; e-mail: irisale@hc.edu.uy

Introductory Course on the Biology of the Skin
10–14 December, 2001, Downing College, Cambridge, UK

This course is primarily for registrars and postgraduate students at an early stageof their training in dermatology but it is open to other interested practitioners. Closing date for applications is 9 November, 2001. For further information please contact: Postgraduate Medical Centre, Clinical School, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2SP, U.K. Tel.: +44 01223 217 059;
e-mail: sw318@medschl.carn.ac.uk

Announcements

Mount Sinai School of Medicine Symposium

Call for abstracts

Abstracts are invited for a 3-day symposium, 'Advances in Medical and Surgical Dermatology', to be held 79– December 2001 in New York, USA. Closing date for abstracts is **1 November, 2001**. The timetable for the meeting is as follows:

Friday December 7: Surgical meeting. Cutting edge lectures on all aspects of surgical and cosmetic dermatology:

Saturday December 8: Live patient demonstrations of filler substances, Botox, laser treatments. Scientific meeting lectures by leaders in dermatological research. Prizes of $500, $250 and $100 will be awarded for the best three poster abstracts.

Sunday December 9: Medical meeting. State-of-the-art lectures on psoriasis, atopic dermatitis, STDs, skin manifestations of HIV, topical immunomodulators, contact dermatitis.

Reduced registration fee available for dermatologists outside of north America. Further information can be obtained from: http://www.mssm.edu/dermatology/symposium2001, or by contacting Donald Rudikoff MID,
email: RNAhybrid(a)aol.com

British Skin Foundation 2001 Awards: Call for Grant Applications

The Trustees of the British Skin Foundation wish to announce that funding is again available for skin disease research. This year there are four categories of award as listed below. Applicants are asked to apply for funding from the category that they feel is most appropriate. The closing date is **17th September 2001**.

BSF Research Awards: One- or 2-year project grants of up to £50,000 per annum.

The BSF Fellowship: A grant of £40,000 to support a specialist registrar in dermatology through one year of research. Candidates should submit details of their proposed research and a C.V. in the manner described below. Selection will be by interview in late 2001. It is envisaged that the successful candidate will already hold an NTN or will have just completed their training.

BSF Small Grant Awards: One-off payments of up to £10,000. May be used to purchase equipment or for less costly projects.

BSF Studentship: A 3-year package, value £44,000, covering tuition fees, expenses and some consumables.

If you wish to receive an application form for a British Skin Foundation grant, please contact the office, specifying the type of grant you are interested in at:
British Skin Foundation, 19 Fitzroy Square, London WIT 6EH, U.K. Tel: 20 7383 0266; fax: 7388 5263.