LETTERS

Cutaneous cryptococcus *Laurentii* infection in a human immunodeficiency virus-negative subject

To the Editor

Cryptococcosis is an acquired immune deficiency syndrome (AIDS)-related opportunistic infection found in 6–13% of subjects with AIDS.[1,2] The remaining cases are comprised in the group of immunocompromised subjects with other diseases (e.g. underlying malignancy) or who are undergoing immunosuppressive therapy.[3–5] Only rare cases of immunocompetent subjects are described as developing the infection.

We present a case of cutaneous cryptococcosis caused by *Cryptococcus laurentii* in a 51-year-old human immunodeficiency virus (HIV)-negative man. Cutaneous cryptococcosis was the presenting sign of disseminated infection involving the central nervous system manifesting in the form of meningoencephalitis cryptococcica. The man was a surveyor who had done active field-work for many years. Except for being an avid consumer of alcohol, he had no unusual habits; there was no obvious underlying cause of immunosuppression. Two months prior to admission the man had noticed an ulceration on his back that he had treated with hydrocycline; the ulcer had enlarged and additional cutaneous lesions had developed elsewhere. On examination we saw a large erythemolivid plaque in the middle of the man's back. The plaque had a tumour-like appearance with central ulceration and raised and 'rolled' edges. Numerous satellite, papulonodular lesions were noted with two distinct aspects; some had a central area of superficial necrosis, with crusting and comedo-like aspect, while others were shiny, dome-shaped, aggregated, with central umbilication, resembling the lesions of molluscum contagiosum (fig. 1). Several similar small lesions were observed in the axillae and on the neck and face. There was no lymphadenopathy and no involvement of the mucosae.

Routine biochemical and haematological analyses were normal. Serological markers for hepatitis A, B, and C, Cytomegalovirus, Epstein-Barr and HIV viruses, were all negative; the T-helper/T-suppressor ratio was also normal. A chest X-ray revealed subsegmental consolidation in the right hemithorax supradiaphragm with interstitial fibrosis, but the man refused further investigations for this chest finding. Histological examination using haematoxylin and eosin staining showed two forms of tissue reaction in the same skin specimen, i.e. granuloma and gelatinous form. With the periodic acid-Schiff stain, the yeast cells stained positively red (fig. 2) and with alcian blue the organisms stained blue (the pathogen capsule stained dark blue) and were seen contained in cystic formations. A presumptive identification of *Cryptococcus* was confirmed by isolation of shiny light-yellow colonies on Sabouraud agar at 37 °C 48 h after taking the skin smears. Biochemical identification of the culture was made using automated VITEK technology and *C. laurentii* was detected and confirmed sensitive to both amphotericin B and 5-fluorcytosine. Soon after the man's condition worsened; in particular, he experienced severe headaches and vision problems and he was transferred to the infectious diseases ward. Meningoencephalitis cryptococcica was diagnosed.

Cryptococcosis is a rare infection in non-immunocompromised individuals. Except for the man's chronic alcohol abuse and undetermined pulmonary problems, no other obvious cause for immunosuppression could be found. We were unable to determine the source of the infection, although we believe it was work related, as the man's occupation offered numerous possibilities for contact with potential reservoirs of this pathogen. *C. neoformans* (an encapsulated yeast and primary aetiological agent of cryptococcosis) and *C. laurentii* have been isolated from soil world-wide, usually in association with bird droppings (primarily pigeon) as well as in ponds.[6,7] Inhalation

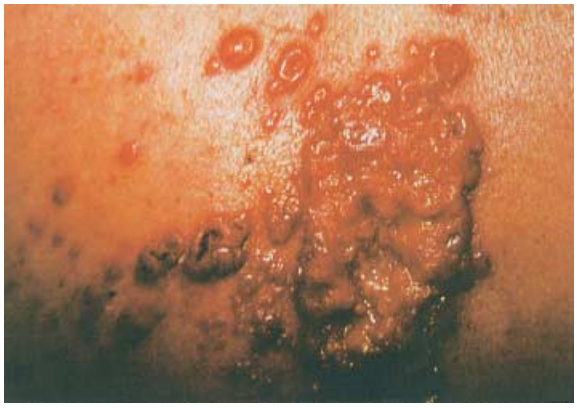

fig. 1 A large tumour-like plaque with central ulceration and small satellite papulonodular lesions resembling those of molluscum contagiosum.

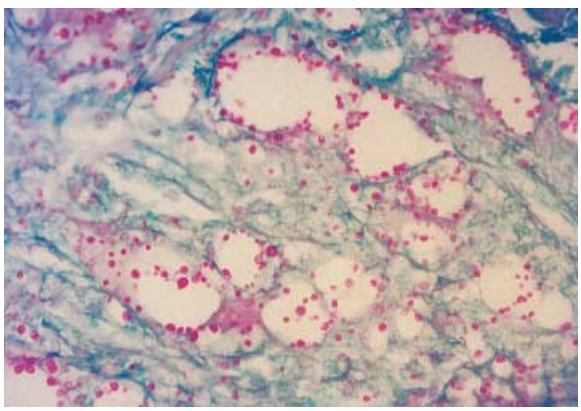

fig. 2 Histological picture (periodic acid-Schiff staining) showing numerous organisms in the cystic formations (gelatinous form); the yeast cells stained positively red.

of airborne yeast and/or basidiospores is the main route of infection. In particular, the man's occupation gives two equally likely possibilities for the probable site of entry of the pathogen, namely, inhalation or a skin wound. If we had had the chance to determine whether the man had already developed systemic infection when he first noticed the lesion on his back, it would have been easier to determine the possible site of entry. In particular, no fungaemia at the time of the emergence of the first cryptococcal lesion, and localized cutaneous lesions could provide evidence for primary cutaneous cryptococcosis.[8] However, similar to other cases of systemic cryptococcosis,[9] as the symptoms of the systemic infection worsened soon after the first lesion was observed (2 months), and the cryptococcal lesions were scattered and emerged soon after the first one, we believe that this man had secondary cutaneous cryptococcosis.

Furthermore, what makes this case unique is the fact that the fungaemia (cryptococcaemia) and cutaneous cryptococcosis were caused by a rather uncommon pathogen, *C. laurentii*, for which there is a paucity of data in the literature. For instance, there are only a few published cases of cutaneous, pulmonary, disseminated and even ocular *C. laurentii* infections, in AIDS and in HIV-negative individuals.[10–12]

This case points out the clinical presentation and characteristics of cutaneous cryptococcosis as monitory manifestation of a disseminated cryptococcal infection, in addition to the 'silent' pulmonary alterations. As scattered cryptococcal lesions are indicators of disseminated infection, they are crucial signs for early and accurate diagnosis of a potentially serious and even fatal disease.

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Tinea capitis by *trichophyton violaceum* in immuno-suppressed elderly man

To the Editor

Tinea capitis is a superficial mycosis caused by dermatophytes, filamentous fungi that invade keratinized structures of the skin and adjoining structures, affecting the scalp and sometimes extending to the eyelashes and eyebrows. These fungi produce extremely variable clinical manifestations,[1] ranging from slight to inflammatory, supurating lesions, depending on the interaction between the host and the ethiological agent. Non-inflammatory *tinea capitis* is a common childhood affliction from the ages of 3 to 7 years,[1] although a few cases have been described in adults from 17 to 76 years of age.[2–8] There is a clear predominance in females[3,5,6] caused by different species of dermatophytes,[9] depending on the geographical location. There is also a difference in temporal incidence as, for example, in southern Spain after the 1936 civil war, the most common forms were *T. tonsurans* and *T. violaceum*, which are currently rare. The most prevalent forms in southern Spain are now those caused by zoophilic species such as *M. canis* and *T. metagrophytes var. metagrophytes*.

We report the case of a patient who was a 77-year-old male with no significant family history and a personal history of prostate cancer, which is currently being treated with 1 mg/8 h

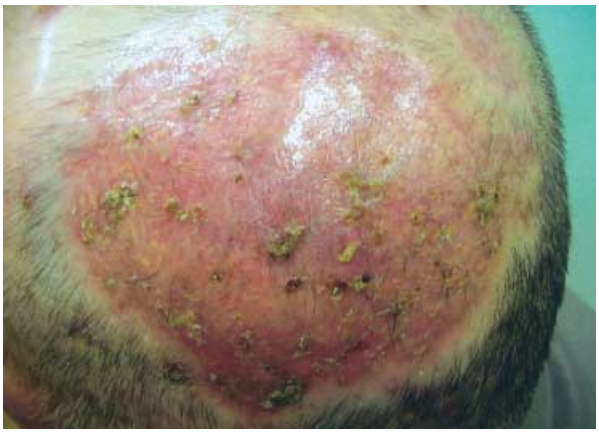

fig. 1 A large alopecic patch 4–5 cm in diameter in the temporoparietal zone.

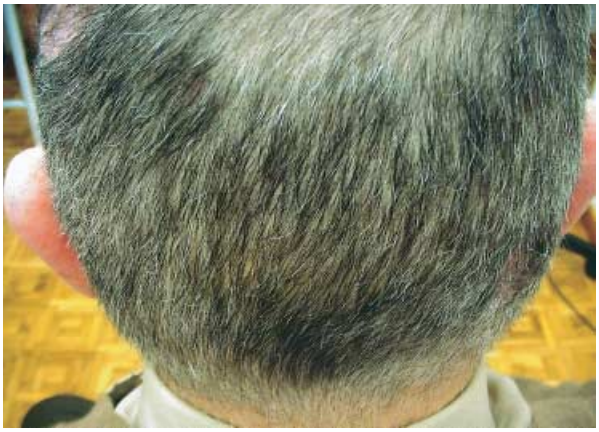

fig. 2 Regrowth was completed by 6 months, with no sequelae from the lesions.

dexamethasone, 10 mg/6 h morphine sulphate, 40 mg daily omeprazole and 30 mg/12 h methotrexate. The patient presented due to several small balding spots, some merging together to form a large patch and having suppurating lesions (fig. 1). These patches were spread throughout the scalp and beard and had been present for several months. In the submaxillary region there were small unattached adenopathies. He had been treated with oral antibiotics and topical antiseptics, with no clinical improvement of the lesions. The patient claimed to have no direct contact with domestic animals and stated there were no similar lesions in family members. The clinical exploration revealed numerous alopecic areas in the vertex area of the scalp and a very large alopecic patch 4–5 cm in diameter in the temporoparietal zone. This spot had broken-off hairs that were easily plucked and papulovesicular eruptions with honey-coloured scabs in the central part, together with follicular pustules. Based on the clinical diagnosis of adult tinea capitis, a sample was taken for culture and mycological study. Direct examination and the culture were positive for *Trichophyton violaceum*, with endothrix-type hair shaft infection and raised, compact colonies, finely branching out and dark violet in colour. Numerous clamidospores were found microscopically. With the clinical and mycological diagnosis of adult tinea capitis, we initiated treatment with 250 mg/day oral terbinafine and topical terbinafine cream at two applications a day. A month after the start of treatment, there was a considerable improvement of the lesions, but the alopecic zones persisted. Treatment was extended for 4 months for his immune status, by which time the cure was completed and the affected zones began to show regrowth of hair. Regrowth was completed by 6 months, with no sequelae from the lesions (fig. 2).

In southern Spain, infection of the scalp by superficial fungi is extremely rare in adults. Incidence ranges from 0.31% to 4.37% of the total dermatophytoses of the scalp in this part of Spain, with a clear predominance in postmenopausal women. For a fungus to be able to develop an infection, an individual must have various predisposing factors and/or several circumstances favouring it, such as: (a) alteration of the cutaneous mucous membrane: traumatism and maceration of the area; (b) decompensated chronic illnesses, such as diabetes mellitus; (c) congenital or acquired disorders of the immune system;[2] (d) age: *tinea capitis* is more prevalent in children since in adults the lipidic layer of the hair contains saturated fatty acids, which have a fungicidal action, this sebum secretion is hormone dependent and does not begin until puberty; (e) inadequate hygiene-sanitary measures; (f) climatic factors, such as excessive dampness and (g) the taking of medication: corticosteroids, immunosuppressants and systemic antibiotics. Several authors have postulated that some endocrine alterations cause an abnormal sebum composition that facilitates infection of the scalp by dermatophytes in adults.[6]

Trichophyton tonsurans is considered to be the species most commonly responsible for cases of tinea capitis in adults in southern Spain.[10] Another species involved is *Trichophyton violaceum*, an anthropophilic dermatophyte that is common worldwide,[9] although more prevalent in north Africa, the Middle East, India and Eastern Europe. This fungus is the causative agent of tinea capitis in both children and adults and occasionally of tinea corporis and tinea unguium as well. Direct examination of the hair reveals endothrix infection of the hair, with septate hyphae and scaly arthroconidias. It is cultivated in Sabouraud's glucose agar (SGA). The colonies grow slowly, in 2–3 weeks, and are characterized by a raised surface and a regular texture, glabbrous or finely branched, typically dark violet in colour. Light microscopy reveals irregular hyphae and arthroconidias.

Diagnosis of both the adult and children's forms is reached through the clinical manifestations.[3] It is then confirmed by a direct microscopy study of a sample of the diseased hairs plucked by tweezers and scales from the area. A culture in an appropriate medium (SGA) is essential to establish the diagnosis by identifying the fungus species.[3] The cultures are

incubated for 30 days. After approximately 2 weeks, the characteristic appearance of the colonies and their typical microscopic morphology can be observed. The use of Wood's light examination, is not needed for *T. violaceum* infection, as this organism does not fluoresece. A skin biopsy of the lesions is not necessary, as the histopathological study will reveal the existence of chronic or subacute dermatitis, with inflammation, follicular destruction and sometimes suppurating folicullitis. The main problem deriving from this illness is the destruction of the hair and of the adjacent pilosebaceous structures, which could cause permanent cicatricial alopecia,[1] with the consequent mental and emotional repercussions for the patient. In severely immunosuppressed individuals, systemic dissemination of the fungus has been described.

The treatment of scalp tineas is carried out with topical antimycotic agents, such as the imidazole derivatives, cyclopirox, naftifine or terbinafine, used in conjunction with systemic treatment with itraconazol, fluconazol, oral triazols, terbinafine or griseofulvine.[4] In addition, an important associated measure is frequent washing of the scalp and affected zones with an acid pH soap or with a 2.5% selenium sulphide shampoo to avoid the risk of the infection spreading by reducing the number of viable spores. It is occasionally necessary to use oral antibiotics and prednisone to prevent permanent alopecia in the inflammatory forms. In our study we opted for terbinafine ace both to local and general medication long term.[4]

The low prevalence of *tinea capitis* in adults and the atypical presentation require a high degree of clinical awareness for its diagnosis.[2] Some authors even consider a possible diagnosis of tinea capitis in any adult patient with scaling of the scalp.[4] A mycological study is essential to avoid late diagnosis and complications. In these patients a long treatment time is required.

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Extensive verruca vulgaris at unusual sites in an immunocompetent adult

To the Editor

We report an immunocompetent adult patient with extensive verruca vulgaris strictly confined to the major flexures.

A 55-year-old woman presented with a 5-month history of progressively increasing multiple, asymptomatic, skin coloured to brown, 2–10 mm, firm, papules with verrucous surface. The lesions were exclusively present in the axillae, groins, medial aspects of the thighs and pubic region (fig. 1). There were no lesions on the labia majora, vagina, perianal region or elsewhere. There was no history of genital ulceration or discharge. There was no past history of any significant illness or intake

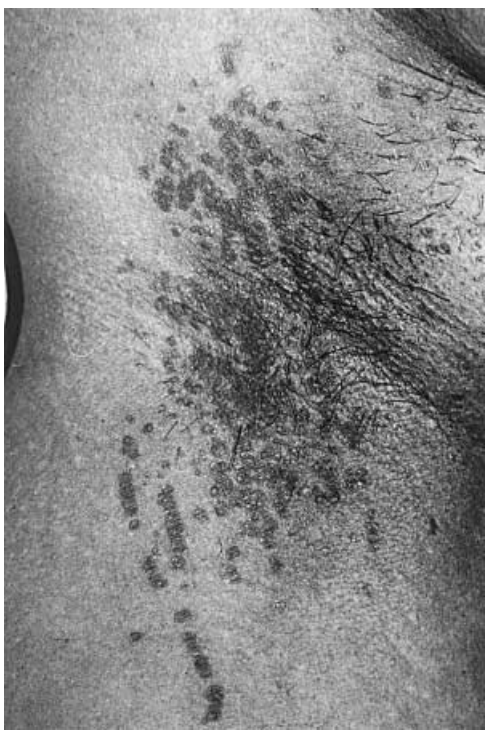

fig. 1 Numerous verruca vulgaris lesions in the pubic region.

of corticosteroids or immunosuppressive drugs or history of similar lesions in her husband or other members of the family.

General physical and systemic examination was within normal limits and gynaecological and per rectal evaluation did not reveal any abnormality. The patient's routine haemogram, liver and renal function tests, blood sugar, urine analysis, stool for occult blood, chest X-ray and ultrasound of abdomen were normal. Enzyme-linked immunosorbent assay test for human immunodeficiency virus infection was negative. Skin biopsy from one of the papules in the right axilla confirmed the diagnosis of verruca vulgaris.

Common warts occur only infrequently on the genitalia, accounting for 1–2% of all warts on or around the genitalia.[1] In males, they are almost always confined to the shaft of penis where they retain their usual morphological characteristics and do not resemble the acuminate (genital) warts.[2] Flat lesions of condylomata acuminata have occasionally been described on the penile shaft, pubic skin and perianal region and groins. These may sometimes be sufficiently pigmented to resemble seborrhoeic keratosis.[3,4] Verruca vulgaris confined to the axillae, groins, pubic region and medial aspects of the thighs is extremely rare.

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The evaluation of the effectiveness and side-effects of a 200-mg/day constant dose of cyclosporin in chronic plaque-type psoriasis: can a constant dose be an alternative?

To the Editor

Cyclosporin A (Cyc-A) is known to be effective in the treatment of psoriasis. However, dose adjustments may cause problems in daily use. In this study, we examined the effectiveness and side-effects of a constant dose of Cyc-A in chronic plaque-type psoriasis.

Twenty-five patients who attended our clinic with both clinical and histopathological features of psoriasis were evaluated. All the patients had active, chronic plaque-type psoriasis lesions and none of them had received any treatment for the past 2 months. One of the patients was excluded from the study after the treatment protocol had started because of elevated liver functions. The study was undertaken with 24 patients, of whom 11 were male and 13 were female. Their ages were between 19 and 66 years (mean age 42.29 ± 13.88 years).

All the patients were evaluated by physical examination every 2 weeks. A course of 200 mg/day Cyc-A (Sandimmune Neoral® caps) was started (with a 12-h interval twice daily), regardless of body weight. All the patients were followed-up for 4 months. According to the clinical result, if successful, the dosage was tapered down by 50 mg/day every 2 weeks.

Only blood-urea-nitrogen (BUN) levels were increased and the psoriasis area and severity index (PASI) score decreased in a statistically significant manner ($P < 0.05$, Wilcoxon signed t rank test). During the study, two patients had insomnia and three patients had hirsutism. Both side-effects were statistically insignificant (χ^2, $P > 0.05$).

Only one patient relapsed in the 1-month follow-up period after the study was finished.

Powles *et al*. studied the effect of Cyc-A on 44 patients and showed that 17 months of therapy with 3.3 mg/kg/day dosage reduced the PASI score in 70.5% ($n = 31$) of the patients.[1] Timonen *et al*. studied 457 psoriatic patients and found that patients taking 2.5 mg/kg/day cyclosporin showed a 59% regression, while the regression rate was 94% in patients taking 5 mg/kg/day at the end of 12 weeks' follow-up.[2] In our study, we found 90% and more decrease in the PASI score in 83.3% of our patients (20 patients). This was similar to results in the literature.

The most serious side-effect of cyclosporin is nephrotoxicity and hypertension. Although the BUN levels were increased significantly in our study, all the values were in the normal range. In addition, we did not encounter hypertension in our patients, except for a patient who was already hypertensive from the beginning. Her blood pressure was normal when using the drug amlodipin.

From the literature it is known that serum lipids, and especially triglycerides, are increased during cyclosporin therapy. Cutaneous malignities are also side-effects of Cyc-A. Hyperbilirubinaemia, hypomagnesaemia and hepatic dysfunction can also be seen in patients who use Cyc-A. One of our patient's hepatic enzymes increased fivefold during the fourth week of therapy. The drug was stopped and the patient excluded from the study. During the follow-up period, the liver enzymes decreased to normal range in a few weeks. Except for this patient, no hepatic side-effects were detected. There are some other side-effects that are not life-threatening but alter the

quality of life, such as tremor, headache, malaise, leg oedema, hirsutism, parestaesia, gingival hyperplasia and anaemia. These effects can be seen in 1–2% of the patients and especially in high dosage users.[3–7] We experienced insomnia in two and hirsutism in three of our patients.

In the review of the literature the dosage of cyclosporin in psoriasis patients is based on the patient's body weight. We aimed to study the effectiveness and side-effects of a constant dose of Cyc-A in psoriatic patients. In conclusion, a 200-mg/day constant dose of cyclosporin was found to be at least as effective as the dosage used per kilogram in the literature on adult psoriatic patients. Our patients did not experience any nephrotoxicity, hypertension or cutaneous malignity. Malaise and hirsutism were detected as minor side-effects. Our result shows that the constant dose cyclosporin therapy is as effective as the conventional usage of the drug. Constant dose cyclosporin is an effective treatment, where no calculation is needed, it is easy to administer and has few side-effects, and provides a time-saving alternative treatment modality during daily dermatological practice.

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Fatal aplastic anaemia in a patient with clarithromycin-induced toxic epidermal necrolysis

To the Editor

Clarithromycin is a macrolide antibiotic used for cutaneous and respiratory system infections with a low frequency of adverse effects.[1] We present a case of fatal aplastic anaemia in a patient with toxic epidermal necrolysis probably caused by clarithromycin intake, which has not been reported previously.

A 65-year-old woman was admitted to our department for a generalized rash, fever and malaise, following the third day of clarithromycin intake. There was no history of clarithromycin intake and allergy to any other drug previously. On physical examination, her temperature was 39.5 °C, pulse rate 98 beats/min and blood pressure 100/60 mmHg. Conjunctivas were hyperaemic, and widespread erosions and ulcerations on oral and genital mucous membranes were detected. Skin examination revealed an erythematous rash that consisted of confluent macules, many of which had the appearance of irregular target lesions distributed on the face, extremities and anterior chest wall covering more than 50% of her body surface area. Nikolsky's sign was positive on lesional skin. Laboratory tests revealed a slight elevation of all liver enzymes; erythrocyte sedimentation rate 38 mm/h (normal range 0–20 mm/h); white blood cell (WBC) count $4.98 \times 10^3/\mu L$ [$(4.5–11) \times 10^3/\mu L$]; neutrophil $3.574 \times 10^3/\mu L$ [$(1.5–6.7) \times 10^3/\mu L$]; haemoglobin 11.2 g/dL (11.7–16 g/dL), haemotocrit 33.3% (35–47%); platelet count $187 \times 10^3/\mu L$ [$(150–400) \times 10^3/\mu L$]. There was no evidence of any bacterial or viral infection. Histological examination of the skin lesions revealed a subepidermal separation of the epidermis and dermis, numerous necrotic keratinocytes, ballooning degeneration and lymphocytic exocytosis in the epidermis. Based on the temporal relationship between drug exposure and the onset of symptoms, a diagnosis of toxic epidermal necrolysis (TEN) induced by clarithromycin was made, and clarithromycin was withdrawn on admission. Methylprednisolone 64 mg/day and, in view of her pyrexia, imipenem 500 mg every 6 h intravenously were started as an empirical broad-spectrum antibiotic therapy. Therapeutic measures also included parenteral nutrition and maintenance of fluid and electrolyte balance with regular skin, eye and mouth care. In the following days, all parameters of the complete blood count gradually decreased. Meanwhile her temperature fell to a subfebrile level and imipenem was stopped on the 10th day of hospitalization. However, on the 14th day her temperature started to increase again and pancytopaenia with marked neutropaenia developed (WBC $0.432 \times 10^3/\mu L$; neutrophil $0.134 \times 10^3/\mu L$; red blood cell (RBC) $3.36 \times 10^3/\mu L$; haemoglobin 9.4 g/dL; platelet count $57 \times 10^3/\mu L$. Therefore, granulocyte colony-stimulating factor (G-CSF; Filgrastim) 48 million units/day subcutaneously and amikacin sulphate 500 mg twice a day and ceftazidime pentahydrate 2 g three times a day intravenously were started. However,

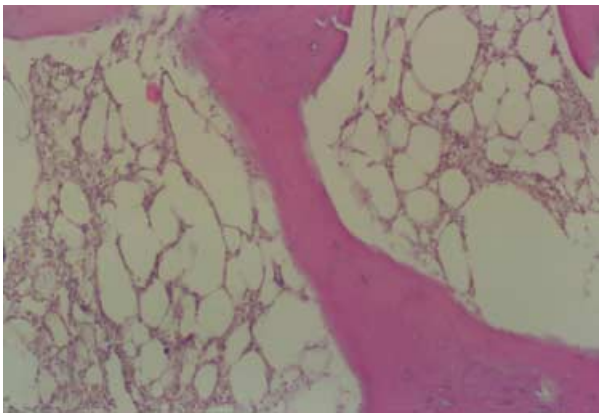

fig. 1 The hypocellular bone marrow (haematoxylin and eosin, original magnification × 100).

a progressive decrease in the complete blood count level continued, and a bone marrow biopsy showed that the marrow was largely occupied by adipose tissue and the cellular component had decreased (fig. 1). The patient's condition gradually worsened and she developed cardiopulmonary arrest on the 22nd day of hospitalization. She was transferred to the intensive care unit, but after 3 days she died.

TEN is a rare, life-threatening, acute mucocutaneous intolerance reaction, usually representing a hypersensitivity reaction to drugs, but it may also be caused by a variety of infections, or have no clear cause.[2] The most common offending drugs are nonsteroidal antiinflammatory drugs (NSAIDs) sulphonamide antibiotics, anticonvulsants and allopurinol.[2,3] The exact pathogenesis of the disease remains unknown, but it is regarded as a cytotoxic reaction aimed at the destruction of keratinocytes expressing foreign antigen.[2,4]

Aplastic anaemia is a clinical syndrome characterized by insufficient production of marrow cells, bone marrow hypoplasia and pancytopaenia. Most cases of aplastic anaemia are acquired. The disorder can be induced by some drugs such as chloramphenicol, phenylbutazone, gold salts, penicillamine and carbamazepine.[4,5]

Although TEN and aplastic anaemia affect different organs, they may share a similar aetiology, at least in some cases caused by drugs. The cellular immunological mechanism plays a substantial role in both TEN and acquired aplastic anaemia.[2,6] Although some haematological abnormalities may be seen in the course of TEN, such as anaemia, neutropaenia, lymphopaenia and thrombocytopaenia,[7] acquired severe aplastic anaemia associated with TEN has been reported in only one case in the literature.[4]

The patient described herein developed TEN soon after the start of treatment with clarithromycin, suggesting the possibility of a triggering effect of this drug. Although imipenem cannot be excluded as an aetiological agent in aplastic anaemia, it is most probable that the immunological mechanism evoked by clarithromycine that led to TEN is also responsible for the occurrence of aplastic anaemia in our patient.

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Scabies in the elderly

To the Editor

Scabies can show atypical signs or symptoms in the elderly due to a different immunological response; therefore, diagnosis is frequently overlooked.[1,2] Scabies epidemics are very common in nursing homes.[3] We present three cases of scabies in the elderly.

Case reports

Patient 1

A 90-year-old woman was hospitalized to evaluate a skin eruption with severe itching of 1 month's duration. At this time a nosocomial outbreak of scabies had been noted in our hospital. Examination revealed papulovesicular lesions on the abdomen

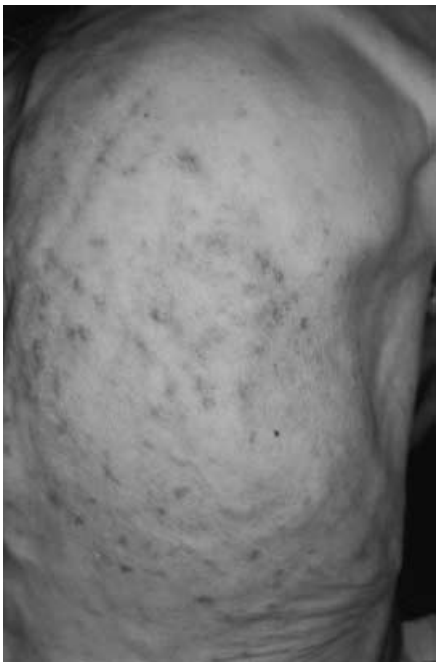

fig. 1 Papules and papulovesicular lesions on the back.

and erythematous plaques on the axillas and groins, but no evidence of burrows. Routine laboratory tests showed eosinophilia. Microscopic examination of scales obtained by skin scraping was negative. We suspected scabies and 5% permethrin cream was given. Cure was observed in a few hours.

Patient 2

During hospitalization in the Traumatology service due to a hip fracture, an 88-year-old woman also presented with severe pruritus and clumps of red papules on the trunk and some burrows on the forearms. She was resident in a psychiatric hospital and had been previously diagnosed with scabies. Re-infestation by *Sarcoptes scabiei* was suspected and proven by microscopy examination of scrapings. We recommended isolation and treatment with scabicides (5% permethrin) not only to the patient, but all symptomatic and asymptomatic contacts.

Patient 3

A 75-year-old woman from the same ward and psychiatric hospital as case 2 was referred to us because of pruritus and skin eruption. On examination we observed papules on the abdomen and back (fig. 1) and burrows on the palms (fig. 2). Microscopic examination demonstrated many mites and eggs. Five per cent permethrin cream treatment to the patient and contacts was indicated.

Scabies is a cutaneous parasitosis caused by the mite *Sarcoptes scabiei* var *hominis*. Affected persons have pruritus usually with

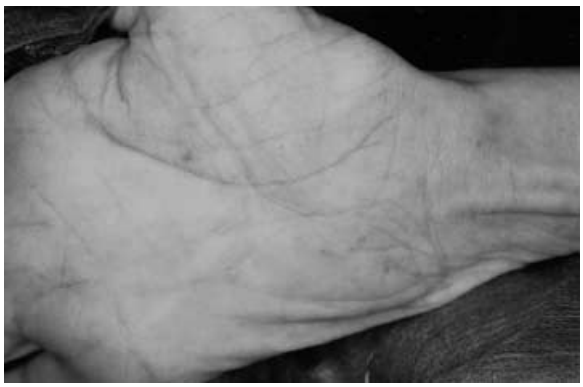

fig. 2 Burrows on the palms.

nocturnal exacerbation. Lesions consist of burrows, papules and nodules on the axillary folds, nipple areola, peri-umbilical area, buttocks and thighs. Secondary lesions may be found. Inappropriate use of topical steroids may modify the clinical picture mimicking other dermatosis (scabies incognito).[4,5]

Skin ageing and disturbed inflammatory response contribute to an atypical presentation of scabies in the elderly. Papules clustered on the trunk can be observed instead of burrows on the hands, or typical burrows may be seen on unusual sites. Lesions can be very keratotic or can be localized on the face, scalp, palms, soles, elbows, knees and buttocks. The back is frequently involved in these cases compared with the rare involvement at this site in young patients. This is why scabies in the elderly may be mistaken for other skin diseases such as psoriasis, eczema, exfoliative dermatitis, drug reactions or contact dermatitis.

According to Lyon and Fitzpatrick, three clinical variations of scabies may be distinguished in the elderly:[1] (i) cryptic cases with pruritus but only minimal lesions; (ii) scabies incognito; and (iii) Norwegian or crusted scabies containing huge number of mites.

Several nosocomial scabies outbreaks have been observed in recent years. The lack of clinical suspicion for atypical scabies in the index patient, often in elderly individuals, have resulted in the epidemic.[6]

Permethrin is a pyrethroid synthetic with a very strong acaricide activity, which is proved to be safe, effective and well tolerated. The probability of systemic effects is 40–400 times lower than with Lindane 1%,[7] which is why we have been using this drug on our patients. A single oral dose of ivermectin (0.2 mg/kg) has shown to be effective and well tolerated.[8] This treatment seems of great interest in particular varieties of scabies (crusted scabies, immuno-compromised patients) or in the case of community epidemics[9].

In conclusion, we agree with Fraser-Andrews *et al.*,[10] who have recently reported three cases of scabies with clinical and histopathological atypical features, in that we must keep a high level of suspicion of this infestation and consider this diagnosis in any elderly patient with pruritus.

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Localized mucinosis subsequent to erysipelas

To the Editor

Erysipelas is a frequent cutis infection usually elicited by Group A, β-haemolytic Streptococci.[1] The diagnosis is orientated to the main symptoms of erythema with flame-shaped offshoots, fever and general malaise. Therapeutic success can be assessed clinically on the basis of regression of the signs of inflammation. Here we are reporting several cases of erysipelas in which persistent infiltrated erythema in the area of the erysipelas gave rise to a suspicion of therapy resistance. In each case, localized mucinosis was determined histologically.

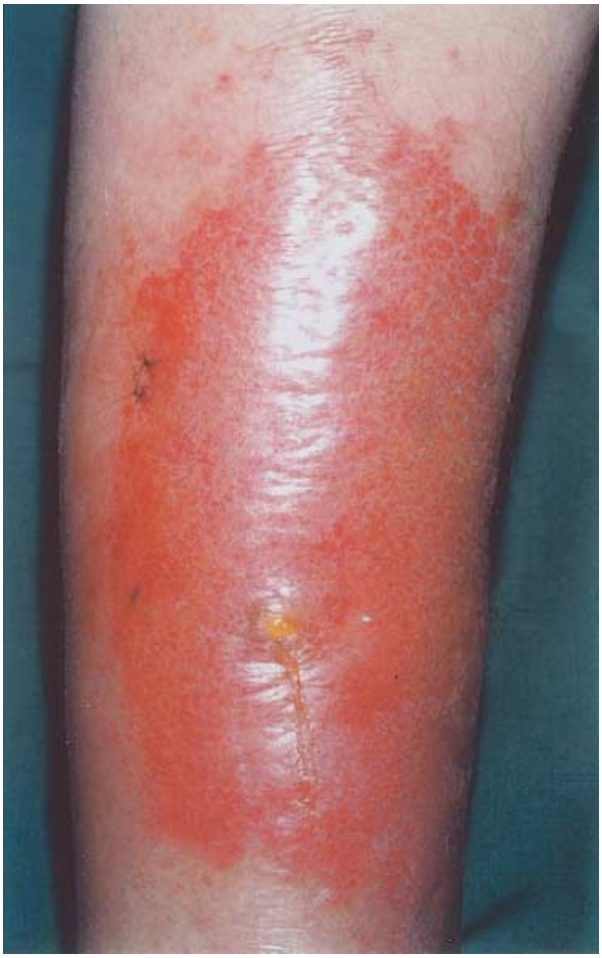

fig. 1 Pretibial mucinosis following erysipelas in a 66-year-old woman.

Between 1996 and 2001, out of 180 patients with erysipelas receiving inpatient treatment in our hospital, seven female patients (3.9% of all erysipelas patients) developed clinically evident localized mucinosis in the course of the disease. The mean age was 64.7 years (± 17.8 years). Chronic lymphoedema was present in three women, the others had previously been free of skin events.

Intravenous antibiotic therapy with 3 × 10 Mega Penicillin G initially resulted in marked improvement in general well-being in all cases. Clinically, however, infiltrated, sometimes pad-like, yellow erythemas persisted in the area of the previous erysipelas (5 × lower calf, 1 × foot, 1 × upper arm) (fig. 1). These covered only part of the area affected by erysipelas. Under the assumption of therapy-resistant erysipelas, a switch was made to other antibiotics without any effect. Skin biopsies taken in all cases because of the persistent erythemas revealed pronounced accumulation of acid mucin in the papillary dermis (fig. 2).

In further examinations to identify the possible cause of mucinosis, latent hyperthyreosis (reduced values of the thyroid-stimulating hormone) was diagnosed in two patients. The thyroid parameters were unremarkable in the other cases. In one case a

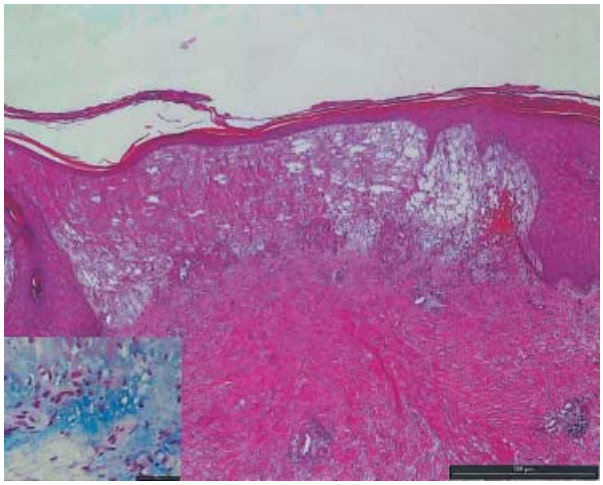

fig. 2 A 66-year-old woman. Haematoxylin–eosin stain. Subepidermal blister and plate-like mucinosis in the Stratum papillare. Inset: Colloidal iron stain, evidence of acid mucins.

first diagnosis of a previously unknown systemic scleroderma was made. The localized mucinosis gradually abated in all cases under local therapy with corticosteroids and compression.

Localized mucinosis subsequent to erysipelas has not, to our knowledge, yet been described. However, there are reports in the literature of the early twentieth century of changes in collagen connective tissue in erysipelas. In 1921, Unna described the transformation of the collagen connective tissue to a 'homogeneous mass … (which) progresses to a maximum state of softness, from which an extremely hard-to-stain pulp forms which is only amenable to resorption' (cited in [2]). This probably first evidence of erysipelas-associated mucinosis was especially observed following facial erysipelas. Considering this description, it seems possible that mucinosis is occasionally (perhaps always subclinically?) associated with erysipelas. The pathomechanism that led to mucinosis is unknown. Both pathological stimulation of fibroblasts and impaired removal by the lymphatic vascular system appear possible. Although we found latent hyperthyreosis in two patients and systemic sclerosis in another, no definite relationship between these diseases and the mucinosis can be concluded. Furthermore, the topographical pattern of mucin deposition (accumulation in the Stratum papillare) in our cases does not correspond to pretibial myxoedema, which is characterized by mucin accumulation in the lower dermis segments.[3] The essential factor in the onset of mucinosis seems, however, to be reduced lymphocapillary drainage. These considerations are supported by the histological agreement of our patient findings with those of Somach *et al.*,[3] who also found mucin deposition in the papillary dermis in patients with stasis dermatitis. During erysipelas, lymphocapillary stasis is caused by an increased lymph-dependent load, while the transport capacity decreases due to spasms, paralysis or destruction of the lymph vessels.[4]

There is still no gold standard for the therapy of mucinosis; it consists primarily in the recognition and treatment of any underlying diseases. In addition, local treatment with glucocorticoids (intralesional or as foil bandage) and compression may be made,[5] and these were also successful in our patients.

In summary, it can be stated that localized mucinosis mimics the prolonged course of erysipelas. Mucin deposition seems to be a result of impaired lymphocapillary drainage.

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Bullous lichen sclerosus atrophicus

To the Editor

Lichen sclerosus et atrophicus is a rare, chronic, mucocutaneous disease of unknown aetiology. Onset can occur in subjects of any age, but the condition is more prevalent in adult females around the time of menopause than in males. The most common site of the lesions is the anogenital area. The usual symptoms are soreness and pruritus. Bullous lichen sclerosus et atrophicus is an unusual form of the disease and the exact prevalence is uncertain.

We report the case of a 53-year-old woman who had been complaining of perineal burning and itching for about 1 month. Except for these symptoms she felt healthy and presented no associated immunological diseases. Physical examination revealed porcelain-white, atrophic, parchment-like changes on the inner side of the labia majora and an erythematous area with purpuric lesions, small telangiectasias and a serohemorrhagic bulla on the perineum. No other pathological lesions were observed on the woman's skin or mucosa.

Routine biochemical and haematological analyses were normal. Unfortunately, for financial reasons we were not able to perform the immuno-serological tests. Examination of a bioptic specimen from the involved perineum indicated a diagnosis of lichen sclerosus et atrophicus and we initiated treatment with topical corticosteroids in the morning and oestrogen in the evening. During the first month of therapy the pruritus disappeared; 3 months later the woman developed new tiny, linear, ivory coloured, atrophic lesions on the intergluteal cleft but from then until now, 6 months later, the woman has been free of pruritus and no new bullae have appeared although the old lesions have not resolved completely.

Many factors, such as low sex hormone output, Borrelia infection, chronic infections and trauma, have been suggested as triggering factors for lichen sclerosus et atrophicus. The increased prevalence of organ-specific antibodies and of associated autoimmune diseases suggests an autoaggressive aetiology. A very interesting scenario was reported in the correspondence published last year in the *Journal of the American Academy of Dermatology*. Carlson and Murphy[1] suggested that loss of androgen receptor expression in lichen sclerosus may be a secondary phenomenon due to a change in squamous phenotype rather than to hormonal pathogenesis. On the contrary, Clifton and Smoller[2] proposed that lichen sclerosus represents a focal androgen insensitivity, as a result of random inactivation of the androgen receptor gene. This inactivation may be triggered by koebnerization, local infection, inflammation or any of the other previously described associations with disease onset and leads to receptor loss with disease progression. In their opinion early treatment with topical testosterone may bind and stabilize remaining receptors leading to regression of the lesions. If treatment is delayed inactivation continues and a new phenotype is expressed that no longer responds to topical testosterone because all receptors have been lost.[2] In addition to these hypotheses, we found in the literature a small study about the localization and level of androgen, oestrogen and progesterone receptor expression in lichen sclerosus and in normal vulvar skin. Androgen receptor was expressed in 12.8% of tissue specimens of lichen sclerosus, oestrogen receptor in only one patient, and progesterone receptor in none.[3] These data show that there is no evidence to date in support of the exclusive role of any single factor in the pathogenesis of lichen sclerosus et atrophicus.

Vulval bullous lichen sclerosus et atrophicus may be misdiagnosed as cicatricial pemphigoid, amelanotic malignant melanoma, leukoderma or candida infection. In children it can mimic (or be misdiagnosed as) sexual abuse. It has been reported that bullous lichen sclerosus et atrophicus has appeared on a morphea lesion. In such cases one must search for lesions elsewhere on the trunk.

Lichen sclerosus et atrophicus is a chronic condition with signs and symptoms that may wax and wane. Progression to destructive scarring is common, but it is more important to know that involved subjects face an increased risk of developing vulvar or penile cancer.[4,5]

The treatment of choice for anogenital lichen sclerosus et atrophicus is local application of a potent topical corticosteroid for a limited time. Estrogen- or testosterone-containing creams and topical retinoids can also be used. Circumcision may be indicated in men, and surgery in women.[4,6] Surgical therapy is indicated when the lesions present signs of malignant transformation or when medical treatment has failed; the three main surgical procedures are vulvectomy, cryosurgery and laser ablation.

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Thyroid function and autoimmunity in children and adolescents with vitiligo

To the Editor

Vitiligo is a common disease that affects 0.5%–1% of the human population, and it is more prevalent in females than males. The disease manifests before 10 years age in 25% of cases (and in infants as early as 4 months of age), before 25 years in 50%, and after the fortieth year in only 10%–15% of subjects.[1,2] The frequent association of vitiligo with autoimmune thyroid disease (ATD) is well known.[1,3–5] The aim of this study was to

assess the prevalence of thyroid dysfunction and autoimmunity in children and adolescents with vitiligo.

We studied 61 children and adolescents with vitiligo, 35 girls and 26 boys, 1.16–16.16 years old; the ages at the time of onset of the disease varied from 0.32 to 16.16 years and disease duration ranged from 0.08 to 11 years. Family history was assessed in 37 children and adolescents with vitiligo. The clinical variants were as follows: vitiligo vulgaris, 54 (focal, eight; extensive, two; stable, 36; progressive, eight) and halo nevi, seven. The size and consistency of the thyroid gland, heart rate, arterial pressure and skin humidity were evaluated. Thyroid function tests included base levels of T3, T4 and TSH (FIA, Delfia) in 58 children and adolescents with vitiligo. TRH test was performed in 22 children. Antithyroglobulin (TAT) and antimicrosomal antibodies (MAT) were evaluated in the 58 children and adolescents with vitiligo (microhaemagglutination method). Ultrasound examination of the thyroid gland (7.5 MHz transducer) was carried out in 44 children. Cellular and humoral immunity indices were evaluated in 15 children with vitiligo and 26 control children. Variation analysis (Student-Fisher's *t*-test) and graphic analysis were used.

There was a family history for thyroid disease in 16 of 37 children, diabetes mellitus in 22 of 37 children, vitiligo in eight of 37, alopecia areata in five and rheumatoid arthritis in two. There was a two-fold female prevalence of thyroid disease and diabetes. Thyromegaly was present in 31 children (23 girls and eight boys), 17 with degree IA, 11 with degree IB, and three with degree II. The thyroid consistency was soft in 23 children (74.5%) and firm in eight (25.8%). The skin was normally moist in 39 children, dry in nine and excessively moist in two children with thyrotoxicosis. An accelerated heart rate and increased blood pressure were registered in only two children with thyrotoxicosis. Thyroid function was assessed in 58 children and adolescents with vitiligo with the following findings: hyperthyroidism in three children, subclinical hypothyroidism (SH) in five and euthyroid function in 50 ($P < 0.001$) (Table 1). TRH test carried out in 22 cases showed a hypothyroid type response in six children and a normal response in 16 (72.7%). TAT and MAT titres were increased in 29 children (fig. 1). Ultrasound examination of the thyroid gland revealed abnormalities typical for autoimmune thyroiditis (AT) in four children, suggestive for AT in 11 and typical for thyrotoxicosis in two. ATD was diagnosed in 32 children (29 children with AT and three with thyrotoxicosis). Neck lymphadenopathy was found in only four children. The evaluation of the cellular and humoral immunity parameters in children with vitiligo and AT revealed decreased numbers of cytotoxic Ly (TLy), an increase of activated TLy and decreased cells with natural killer activity ($P < 0.001–0.01$).

Table 1 T3, T4 and TSH levels (mean ± SD) in children with vitiligo

	T3 nmol/L X ± SD	T4 nmol/L X ± SD	TSH mIU/L X ± SD
Healthy children (controls)	2.02 ± 0.58 *n* = 118	118.2 ± 21.12 *n* = 138	1.88 ± 0.87 *n* = 162
Children with vitiligo and normal thyroid function	3.24 ± 0.94 *n* = 11 *P* = NS	117.9 ± 19.44 *n* = 41 *P* = NS	1.66 ± 0.65 *n* = 50 *P* = NS
Children with vitiligo and subclinical hypothyroidism	3.16 ± 1.22 *n* = 3 *P* = NS	133.92 ± 12.24 *n* = 4 *P* = NS	5.41 ± 1.67 *n* = 5 *P* < 0.001

It is still unclear why vitiligo manifests as spotty depigmentation (segmental, symmetric or total) in the presence of autoantigen against all melanocytes. The greater incidence of vitiligo in females in our study correlates with the commonly accepted view.[2] The family prevalence of a number of autoimmune endocrine and systemic diseases in vitiligo supports the hypothesis for its autoimmune genesis. The presence of thyromegaly, antithyroid antibodies and thyroid dysfunction in significant numbers of our patient cohort indicates frequent involvement of the thyroid gland in vitiligo, as reported previously.[6–8] Some authors have observed that thyroid gland involvement in vitiligo increases with age,[9] while others have reported no correlation between functional thyroid disorders, patient's age and the duration of vitiligo.[8] There was no correlation between the positive titre of thyroid antibodies and the abnormal TRH responses in our vitiligo subjects, contrasting with the findings reported by Betterle.[10] The fact that in 40% of cases we found an atrophic type of autoimmune thyroiditis is of interest. The finding that the thyroid function abnormalities in our children were

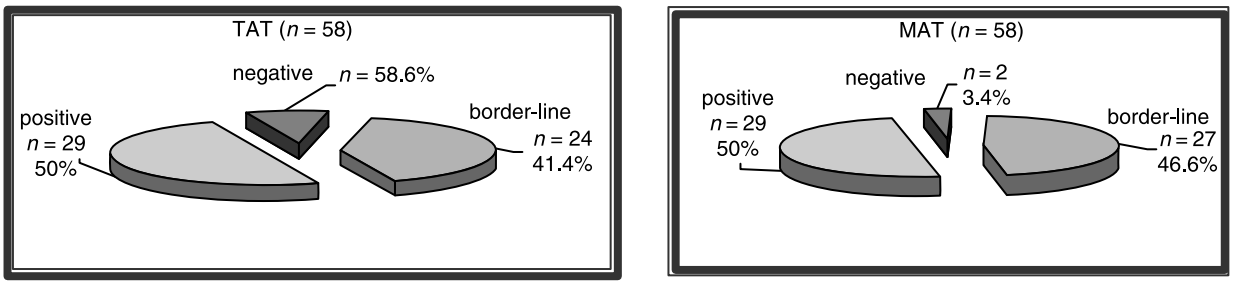

fig. 1 Thyroid auto-antibodies in children with vitiligo.

subclinical emphasizes the need to assess thyroid function in subjects with vitiligo. The changes in the indices of cellular immunity in our children suggest the participation of several types of TLy in the pathogenesis of the autoimmune process in vitiligo. The increase of activated TLy in the peripheral blood and the presence of infiltrates of these lymphocytes in the skin and the thyroid gland in vitiligo subjects is well established. It has been suggested that the epithelial cells express the aberrant HLA-DR antigen.[4] Our study emphasizes the prevalence of thyroid gland pathology in children with vitiligo.

We recommend that thyroid gland function be assessed annually in children with vitiligo. The early diagnosis of clinical and subclinical forms of thyroid disease in these children facilitates early treatment and avoidance of the phenotypic manifestations of hypothyroidism.

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UVB phototherapy for Pityriasis rosea

To the Editor

Pityriasis rosea (PR) is a common, self-limiting, eruptive erythemo-scaling disease that begins with the appearance of an initial plaque most often on the trunk, followed in about a week or two by the development of an analogous spotty rash.

The aetiology of the disease is still unknown (probably viral),[1] and it cannot be treated causally. Merchant and Hammond in 1974[2] were among the first to promote the idea of the therapeutic effect of ultraviolet (UV)B rays on PR but the reports concerning this problem are still few.[2–7]

In the present study we wanted to verify the therapeutic effect of UVB rays on PR and to devise rapid and successful methods for UVB phototherapy of the disease.

The study included 101 patients: 53 (52.5%) women, 34 (33.7%) men and 14 (13.9%) children. All were in good health, with no data for photosensitivity and with negative serological tests for syphilis. The duration of the disease before the beginning of the treatment varied between 7 and 25 days. The patients were with phototype II–IV. In seven of them (6.9%) irritation of the rash was observed.

The severity of the disease was determined according to the Pityriasis Rosea Severity Score (PRSS).[6] Three target symptoms – erythema, infiltration and scaling – were assessed with the use of a scale from 0 to 3. Depending on PRSS values the patients were divided into two groups; those with light to moderate (PRSS < 15) and those with severe (PRSS > 15) forms of PR. To assess any effect of the UVB phototherapy the index was determined at the beginning and at the end of the treatment.

The irradiation sessions were held in a conventional UV cabin (Waldmann 7001 K). Two groups of patients were formed. The first one comprised 24 (23.8%) people. The initial dose of the irradiation was 80% minimal erythema dose (MED). It was increased according to the degree of the preceding erythema. Only the right half of the body was irradiated with UVB. UVA (1 J/cm^2) was given as a placebo to the left half of the body (Table 1). The second group consisted of 77 (76.2%) patients. The UVB irradiation was applied to the whole body. The initial UVB dose was determined according to the phototype (Table 1).

The procedures were held four times weekly. During the treatment course the patients did not receive any systemic

Table 1 UVB dosage in Pityriasis rosea therapy

UVB dose (J/cm^2)	Ist group *n* = 24	2nd group *n* = 77
Initial	80% MED	0.06 phototype II 0.08 phototype III–IV
Increase in dose		
No erythema		+20%
Slight erythema		Same dose
Intense erythema		No irradiation

Table 2 Results from UVB phototherapy of PR

PRSS	PRSS values		Number of procedures	Mean dose UVB in J/cm²
	before phototherapy	after phototherapy		
< 15 (n = 72)	9.01 ± 3.76	0	4.7 ± 2.3	0.62 ± 0.42
> 15 (n = 29)	20.69 ± 6.9	0	6.8 ± 2.9	1.12 ± 0.68
Total (n = 101)	12.37 ± 6.9	0	5.3 ± 2.7	0.76 ± 0.55

drugs. The topical therapy included only emollients to prevent skin dryness.

Our experience confirmed that the UVA irradiation in the dose mentioned earlier had no effect on the course of the disease but significant clinical improvement according to PRSS ($t = 17.9$; $P < 0.001$), with total clearing of the rash was observed after UVB phototherapy (Table 2). The analysis of the data showed a statistically significant difference between the mean number of procedures ($t = 4.47$; $P < 0.0001$) and the mean dose of UVB ($t = 3.85$; $P < 0.0001$) necessary for total recovery of patients with PRSS more than and less than 15. The procedures and the dose of UVB increase with the severity of the disease. It is worth noting that in one woman in whom intensive erythema was observed after the first irradiation, no continuation of the treatment was necessary and the rash cleared with only one procedure.

The correlation analysis confirmed the connection between the duration of the disease and duration of UVB therapy ($r = 0.18$; $P = 0.05$). The number of procedures necessary for total recovery could be determined with the help of regression analysis (linear model: $y = a + bx$). The following equation could be used:

$$\text{Number of procedures} = 4.34 + [0.05 \times \text{duration of the disease (in days)}].$$

No significant side-effects were noted during the treatment course except for slight tenderness and dryness of the skin.

The present study demonstrates that the application of broadband UVB in patients with PR substantially decreases the severity of the disease and can result in total recovery. UVA irradiation did not change the course of the disease. This is not surprising as it is known that 1000 times greater doses of UVA are necessary to reach the effect of UVB.

The results presented are in accord with previous bilateral comparison studies in which 5–10 consecutive erythemogenic UVB exposures resulted in decreased extent of the disease.[3,6] The established correlation between the duration of PR and the number of procedures necessary for total recovery confirms the observations of other authors.[3]

The necessity of a greater number of UVB sessions in patients with more severe forms of the disease may be due either to greater values of PRSS or to a higher phototype or the presence of lesions on the lower extremities that are in general more resistant to UV light.

The aetiology of PR is still unknown, as is the mechanism of the therapeutic effect of UVB irradiation. Some authors presume that a cell-mediated immune mechanism with increased numbers of Langerhans cells may be important in PR pathogenesis.[8–10] The suppression of cell-mediated immune response and modification of the number and function of Langerhans cells in the skin following UV irradiation may at least partly explain the beneficial action of UVB light on this disease.

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Discoid lupus erythematosus: clinical and pathological study of 24 patients

To the Editor

From 1996 to 2001 we examined in our department 24 subjects with discoid lupus erythematosus (DLE) (19 females and 5 males, age range 22–77 years, average age 55.5 years), who presented with scalp involvement, most frequently on the vertex (87%). Fifteen of these subjects showed an exclusive scalp localization (fig. 1). The average age of onset of the scalp lesions was 53.6 years and the average duration of the disease 27 months. Nine subjects presented with a single localization on the scalp and 15 presented with multiple localizations. ANA were positive, with a titre of 1 : 160 in one subject, with negative ENA and n-DNA. All the subjects were treated first with topical steroids, and synthetic antimalarials were administered to poor responders. Subjects who did not respond to either of these therapies were treated with oral steroids. Five subjects responded positively to the treatment with topical steroids. The 19 subjects who did not respond were treated with a combination of topical steroids and synthetic antimalarials (during spring and summer, repeated for up to 3 years, as recommended in the literature), and eight of these showed a positive response. The 11 non-responders were treated with oral corticosteroids (up to 0.5 mg/kg/day methylprednisolone or up to 0.5 mg/kg/die prednisone, with rapid tapering), and seven of these subjects showed improvement. Recurrence after suspension of the therapy was observed in 10 cases, limited, however, to cases treated with only topical therapy. Overall we observed an improvement in 15 of the 24 subjects treated.

Direct immunofluorescent examination showed granular deposits of immunoglobulin (Ig)G around the follicles and at the dermo-epidermal junction in 16 of the 24 subjects. DLE is a chronic condition, characterized by neatly demarcated plaques that are red, atrophic, and scaly and on sun-exposed areas.[1]

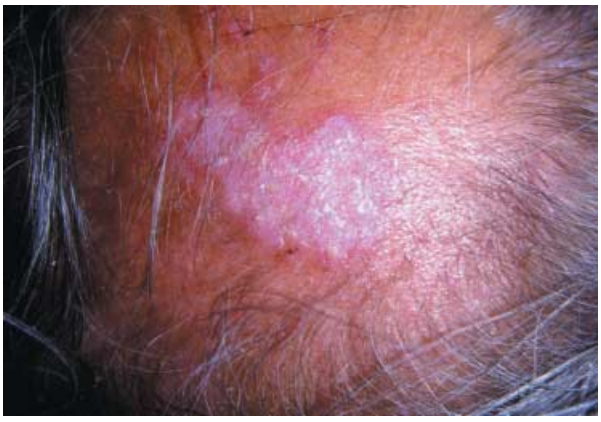

fig. 1 Scarring alopecia due to discoid lupus erythematosus.

This disease represents 40% of all inflammatory conditions causing scarring alopecia.[2,3] The etiopathogenesis is not completely understood, but some of the most probable causes are genetic predisposition, the immune system and other endogenous and exogenous factors.[4,5] The scalp is involved in 30–40% of cases.[5]

When the inflammatory phase fades it leaves a scarring alopecia due to destruction of the follicles by the inflammatory processes. This alopecia can cause aesthetic problems and the chronic forms might degenerate, after a 20–30-year latency, becoming cutaneous neoplasms, including basal cell and squamous cell carcinomas.[6,7]

The therapy is based on the use of topical, intralesional or systemic steroids; synthetic antimalarials are also frequently used as well. In the literature good results have been reported using azathioprine, etretinate, thalidomide and alpha interferon.

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Pigment anomaly caused by calcipotriol in a subject with melanoma

To the Editor

We report the case of a 63-year-old Caucasian male with melanoma who developed naevus spilus-like lentigines following therapy with topical calcipotriol on psoriatic plaques. The man was admitted to hospital in 1998 with a pigmented tumour on his left calf. Excisional biopsy revealed a superficial spreading melanoma (Clark III. Breslow 2.279 mm). After surgical removal of his primary tumour and metastatic lymph nodes, dacarbazine monotherapy was administered for 6 months.

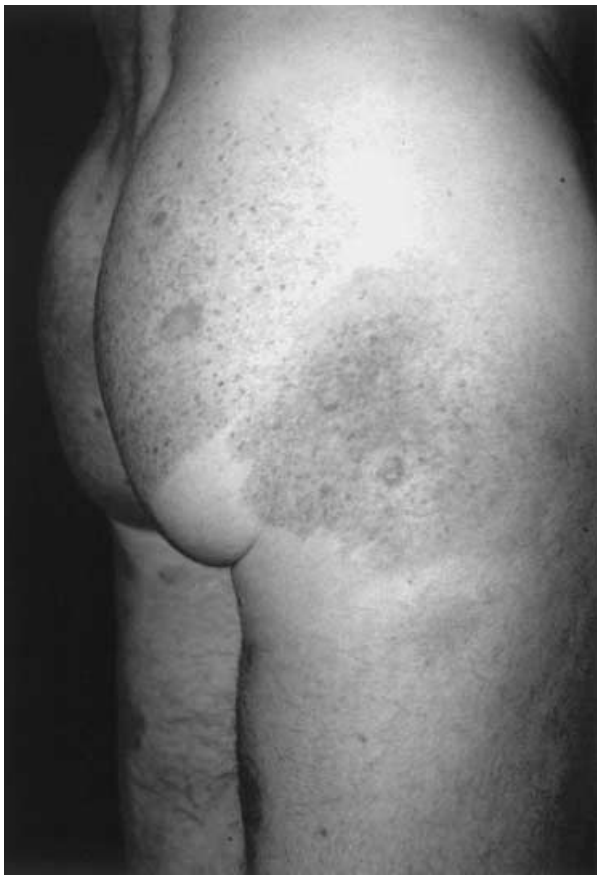

fig. 1 Naevus spilus-like hyperpigmentation in the gluteal region.

The man also had psoriasis, which had started when he was 31 years old. His psoriasis had been treated only with topical steroids, and he had not received phototherapy or any other immunosuppressive treatment. During the chemotherapy his psoriasis worsened considerably, therefore we changed his topical steroid treatment to calcipotriol ointment. Two months after the beginning of calcipotriol therapy, we observed the appearance of small dark brown macules within symmetrical, sharply demarcated, large, light brown macules on his buttocks and extremities (fig. 1). These abnormal, lentiginous skin pigmentations were localized on the psoriatic plaques treated with calcipotriol. A punch biopsy specimen was taken. Histopathological examination evidenced focal melanin pigmentation in the basal layer of the epidermis with hyperproliferation of small vessels and slight mononuclear cell infiltration in the papillary dermis (fig. 2). Gomorri's stain confirmed that the pigment was melanin. No psoriatic change was seen in the specimen.

Two years after the end of both chemotherapy and calcipotriol treatment this lentiginous pigment anomaly is still present.

Calcipotriol is known to cause a local irritative reaction in the skin,[1] which could lead to the development of post-inflammatory pigmentation. The appearance of hyperpigmentation or lentigines have been documented as a side-effect

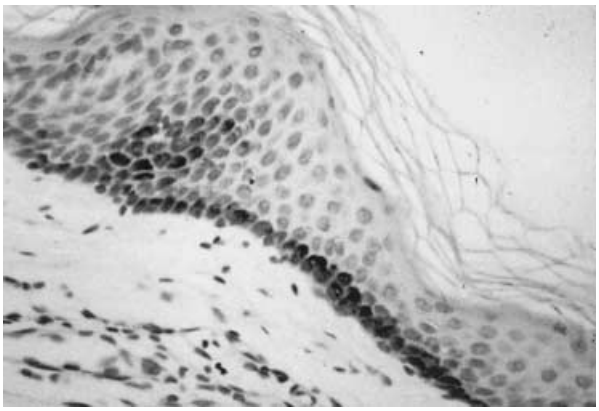

fig. 2 Focal melanin pigmentation in the basal cell layer of the epidermis (haematoxylin–eosin stain).

of phototherapy alone[2,3] or combined with calcipotriol.[4,5] There have also been reports of the appearance of multiple lentigines within healing psoriatic lesions in subjects not treated with PUVA or UV-B therapy.[6] Ours is the first report on the development of lentigines following calcipotriol therapy alone. Some authors have reported that 1,25-dihydroxyvitamin D3 is involved in the regulation of melanin synthesis and melanocytes have been shown to express 1,25-dihydroxyvitamin D3 receptors, but their exact role in melanogenesis is not yet clear.[7,8]

As subjects with melanoma are known to have a tendency to develop hypopigmentation and/or hyperpigmentation,[9,10] it is possible that the calcipotriol caused the pigment anomaly in our patient, and that this was also related to his melanoma.

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Partial response to treatment with recombinant interferon-alpha2a in an adult patient with tufted angioma

To the Editor

Tufted angioma (TA) is a rare benign cutaneous vascular proliferation with typical clinical and histological features. More than 40 of the 260 cases reported in the literature were from Japan.[1] Onset of the disease was below 5 years of age in half of these patients and below 10 years in the other half. Few cases of adult onset have been reported. The treatment of the disease is difficult; surgical excision is often followed by recurrence, and the results obtained with steroids, cryotherapy, radiotherapy and laser therapy are not encouraging. We report the case of a 28-year-old woman affected by tufted angioma and treated with interferon-alpha2a (IFN-α2a). In this case the treatment with recombinant IFN-α2a seemed to be only partially effective.

The 28-year-old woman presented to our department in February 1996 with painful red patches, two of which measured 3 × 2 cm, on the neck. The patches had appeared 2 years earlier and had grown in size. They were roughly oval in shape, raised with respect to the surrounding skin and had well-defined margins (fig. 1). Histological examination of a bioptic specimen showed substantially normal epidermis overlying a proliferation of cells in the middle and deep dermis. The cells were endothelial cells and pericytes arranged in typical 'cannon ball' disposition. Typical 'clefts' were observed in the cell proliferation and their margins. Compact vascular lobules were separated by apparently normal connective tissue. Immunohistochemistry showed positivity for CD31 and actina. A diagnosis of TA was made but the woman refused surgical treatment, which would have been problematic given the site and size of the lesions. She was treated with systemic recombinant IFN-α2a (3 million (international) units (MU) three times a week),

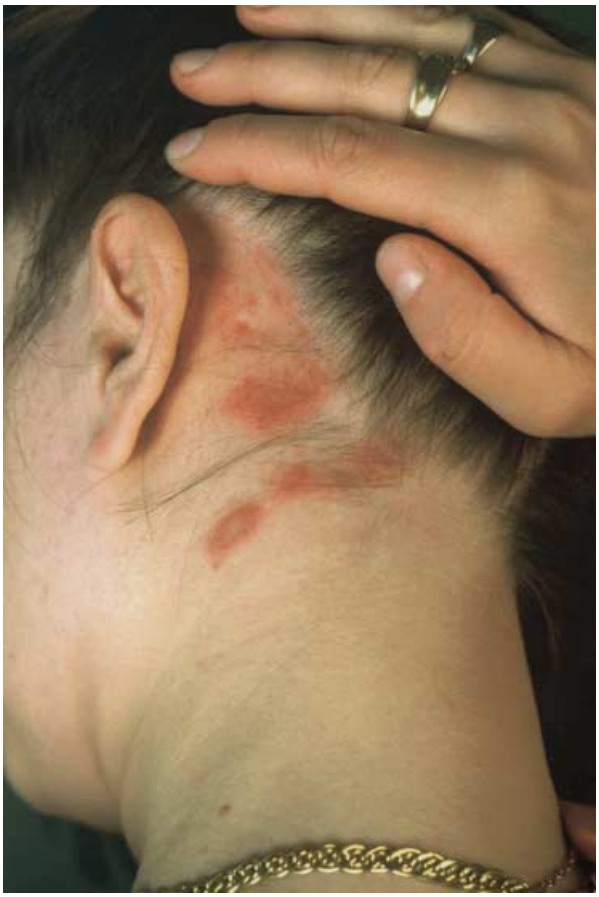

fig. 1 Red patches of angioma on the neck before therapy.

but treatment was suspended after 1 month because of significant side-effects (flu syndrome, headache, abdominal pain, nausea, asthenia). However, the pain ceased and the lateral spread of the lesions was arrested. Treatment was continued with intralesional IFN-α2a (1 MU three times a week for 8 months) without significant side-effects. At follow-up after 1 year the lesions were substantially unchanged.

Tufted angioma, also known as 'progressive capillary haemangioma' or 'Nakagawa's angioblastoma' was first described by Nagakawa as 'angioblastoma' in 1949.[2] In 1976, Wilson Jones introduced the term tufted because of the typical histological pattern of grouped dermal capillary 'tufts'.[3] TA is clinically characterized by the development of painful, bright red, smooth-surfaced macules, papules or nodules with well-defined margins, and by an initial growth phase with lateral extension, lasting from a few months to about 10 years. The most frequent sites are the neck, upper trunk and shoulders. Rarely, TA can regress spontaneously.[4] Differential diagnosis is necessary with special attention to Kaposi's sarcoma, late-onset angiosarcoma, angiomatous eccrine hamartoma and bacillary angiomatosis. Only histological examination allows certain diagnosis of TA. Labelling

of biopsy specimens with anti-*Ulex Europaeus*, antifactor VIII and antivimentin antibodies and enolase (EN4) to identify endothelial cells, and with anti-actin-a antibodies specific for smooth muscle, as well as positivity for CD31, indicate endothelial cell immaturity and the presence of two cellular components (muscle and vascular) in the angioma.[5] The etiopathogenesis of TA is still unclear; however, cases of TA occurring during pregnancy suggest that high oestrogen levels may promote vascular proliferation in TA, as in spider naevi and pyogenic granuloma.[6,7]

As yet there is no elective treatment for TA. Surgical excision is often followed by recurrence, and the results obtained with cryotherapy, radiotherapy and laser therapy[8] are not encouraging. High doses of oral prednisone (2 mg/kg/day) were reported to reduce lesion volume and IFN-α2a was also used when surgery was contraindicated or in life-threatening childhood forms of TA associated with Kasabach–Merritt syndrome and/or refractory to steroid therapy.[9,10] Interferons are a good option for the therapy of some invasive angiomatous diseases, such as haemangiosarcoma, Kaposi's sarcoma and life-threatening haemangioma. The exact mechanism by which these intercellular signalling proteins are effective in vascular diseases is not completely clear. However, it is know that IFNs inhibit migration and proliferation of endothelial cells, decrease platelet aggregation and seem to limit production of factors stimulating angiogenesis, such as basic fibroblast growth factor (bFGF).[11] Partial or complete remission has been obtained in children with TA with administration of subcutaneous or intralesional IFN-α at doses between 0.5 and 3 MU per day or 3–4 times a week for 2–7 months.[5,10–12] To our knowledge, this is the first case of an adult treated with IFN, and the treatment with systemic recombinant IFN-α2a seemed effective, because the pain ceased and lateral spread of the lesions was arrested, but there were major side-effects. Intralesional therapy produced no further significant improvement. We cannot say whether this partial response was due to an insufficient dose of IFN or to low susceptibility of the TA to this drug.

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CagA seropositivity in *Helicobacter pylori* positive patients with psoriasis

To the Editor

Helicobacter pylori (HP) is considered a major pathogenetic factor in chronic gastritis, peptic ulcer disease, gastric adenocarcinoma and low-grade gastric MALT lymphoma. Strains of *HP* that express the cytotoxin-associated gene A (CagA) have been associated with a more virulent disease and may influence the clinical outcome of the infection. Recently, a debate about the association between *HP* and various dermatological conditions, including psoriasis (Ps), has been reported.[1] Although some evidence does not support a strong association between *HP* and Ps,[2–4] the nature of this relationship might differ when the virulence of the infecting strains is examined.

We have investigated, in a prospective case-control study, the seroprevalence of CagA in *HP*-positive patients with Ps.

Eleven patients (eight males, three females, mean age 40.5 years, range 17–63 years) were randomly selected from a total of 62 *HP*-infected patients with Ps. All of the patients, except one with guttate Ps, had the chronic plaque type of disease. Eight of these had a severe disseminated disease involving the head, trunk and extremities. Two patients had psoriatic arthritis. Duration of Ps extended from 3 months to 40 years (mean 19.4 years). Two patients were under treatment with cyclosporin and one with acitretin. Twenty-two sex- and age-matched *HP*-positive subjects with endoscopically confirmed

non-ulcer dyspepsia (NUD), living in the same area, were used as controls. None of the controls had been treated for eradication of *HP* before enrolment, or had Ps. The presence of ulcers or any gross gastrointestinal lesions had been ruled out by endoscopy.

Western blotting using surface antigens of the organisms (Bioblot Helicobacter®, Biokit SA, Spain) was applied to determine serological *HP* infection (positivity of at least 35, 89 or 116 kDa single bands, or positivity of at least two of the 19.5, 26.5 or 30 kDa bands) and anti-CagA *HP* specific immunoglobulin G (IgG) antibodies. To study the association between CagA seropositivity and Ps/controls, Fisher's exact test was used. Informed consent was obtained from all patients and controls.

Six of 11 patients (54.5%) with Ps were CagA seropositive, in contrast to 15/22 (68.1%) NUD controls ($P = 0.47$, odds ratio 0.57, 95% CI 0.1–3.14). CagA status was not associated with duration of disease, type and severity of psoriasis or presence of arthropathy. The two psoriatic patients who were under immunosuppressive treatment (cyclosporin) when the test was performed were CagA positive.

Although most *HP* infections are clinically silent, the organism is associated with substantial morbidity and mortality. Among the known *HP* virulence factors, CagA status is included. CagA-bearing *HP* strains induce a stronger inflammatory response and are strongly associated with peptic ulceration and gastric cancer.[5,6] Although controversial, the association of CagA-positive *HP* infection with different extradigestive conditions such as acute myocardial infection, autoimmune thyroid disorders or rosacea has been reported in case-control studies, suggesting that CagA positive strains might play a role in the development of these diseases.[7–9] In our study, patients with Ps showed a CagA seropositivity of 54.5%, lower than 68.1% of NUD controls (non-significant differences). In a review of the literature, the CagA seroprevalence both in NUD patients and in the general population differ greatly among the geographical localizations. In most of the studies performed in Western Europe, the CagA seropositivity in *HP*-positive NUD patients ranges from 45% to 70%,[10–12] compared with 29% to 61% in the apparently healthy general population infected with *HP*.[10,12,13] It is controversial whether the differences between the two groups of population are significant or not. The CagA seroprevalence of our study is included among the rates of both groups of population, which suggests that the more virulent CagA positive strains of *HP* seem not to be strongly associated with Ps.

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