Montrouge, le 22-06-2015

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Calcipotriol/betamethasone dipropionate ointment compared with tacrolimus ointment for the treatment of erosive pustular dermatosis of the scalp: a split-lesion comparison

paru dans
European Journal of Dermatology, 2015, Volume 25, Numéro 2

John Libbey Eurotext

Table 1. Cases of papular elastolytic giant cell granuloma reported in the literature. "N.D." indicates "not described".

Reference	Sex	Age	Sites of discrete papules or coalscent papules	Coexistence ofannular lesions	Complications	Effect of topical corticosteroid	Effect of oral corticosteroid	Other effective therapies
1	M	55	Trunk, arms	+ (on the trunk)	N.D.	N.D.	N.D.	Intralesional corticosteroid
2	M	75	Trunk, extremities	None	Non-insulin-dependent diabetes mellitus, Hypertension, Osteoarthritis, Anxiety disorder	No improvement	No improvement	Hydroxychloro-quine, quinacrine
3	F	63	Trunk, arms	+ (on the abdomen)	Impaired glucose tolerance	N.D.	Improvement (prednisolone 20 mg)	N.D.
4	M	52	Trunk, extremities	N.D.	N.D.	Improvement	No improvement	N.D.
5	F	53	Neck	N.D.	A history of mastectomy due to breast cancer	No improvement	N.D.	N.D.
6	M	71	Trunk, arms	None	Impaired glucose tolerance	No improvement	N.D.	Tranilast
7	M	71	Trunk, hand	N.D.	N.D.	No improvement	N.D.	Narrow-band ultraviolet B
8	F	43	Neck, trunk	N.D.	Monoclonal gammopathy of unknown significance	N.D.	N.D.	Topical tacrolimus
9	M	62	Trunk	N.D.	A history of gastrectomy due to a gastric ulcer	N.D.	N.D.	Spontaneous regression
Our case	M	75	Trunk, extremities	None	Hypertension, hyperlipidemia	No improvement	N.D.	None

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doi:10.1684/ejd.2015.2521

Calcipotriol/betamethasone dipropionate ointment compared with tacrolimus ointment for the treatment of erosive pustular dermatosis of the scalp: a split-lesion comparison

Erosive pustular dermatosis of the scalp (EPDS) is a rare disorder of uncertain aetiology that mainly occurs on the sun-damaged scalps of elderly patients after trauma.
Topical corticosteroids (TCS) have been widely used in the treatment of EPDS; anecdotal reports have described successful results with topical tacrolimus [1], calcipotriol [2] and dapsone [3, 4]. Nevertheless, due to the rarity of the disease, a comparison of topical treatments in terms

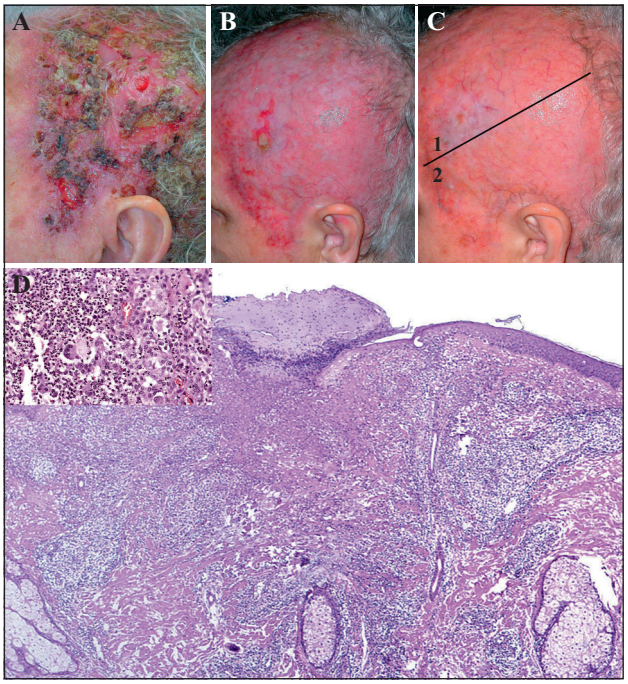

Figure 1. A) Patient before treatment. **B)** Same patient after 3 weeks of treatment with BDCO in the upper half and tacrolimus in the lower half: a small area of persistent disease is observed in the BDCO-treated half which was further treated three times per week. **C)** After three months a complete remission was achieved in the tacrolimus-treated half whereas a small area of residual active disease was still present in the BDCO-treated half, which healed after an additional month of treatment. **D)** A dense infiltrate composed of lymphocytes, neutrophils and occasional foreign body giant cells. Closer examination shows a predominantly neutrophilic infiltrate (haematoxylin-eosin stain; original magnifications: ×10, inset ×40).

of effectiveness and rate of clearing is lacking. Herein we provide a split-lesion comparison of tacrolimus and calcipotriol/betamethasone dipropionate ointments in the treatment of EPDS.

An otherwise healthy 86-year-old woman was referred for treatment of asymptomatic dermatitis involving her scalp *(figure 1A)* of 9 months duration. The lesion onset occurred after CO_2 laser treatment for a warty lesion thought to be an actinic keratosis. Her general practitioner prescribed several courses of antibiotics (2% fusidic acid ointment, amoxicillin (1 g twice daily for 15 days) followed by ceftriaxone sodium (1 g daily for 10 days) and minocycline (100 mg daily for three months)) without any improvement. She was then treated with itraconazole (100 mg daily for 3 months) which resulted in an exacerbation of the condition. A biopsy specimen showed an inflammatory infiltrate consisting of lymphocytes, plasma cells and neutrophils; there was no evidence of malignancy *(figure 1D)*. Direct immunofluorescence and periodic acid-Shiff staining yielded negative results. A diagnosis of EPDS was made. At the time of consultation, the patient was understandably disappointed with the results achieved with the previous systemic treatments. We therefore offered a split-lesion comparison of two topical treatments to quickly identify the most effective agent [5]. Regrettably, topical dapsone is not available in Italy and our patient declined the complex administrative procedure required to obtain the drug. A combination of 0.5 mg/g betamethasone dipropionate and 50 μg/g calcipotriol ointment (BDCO) is available for the treatment of psoriasis, therefore we speculated that a combination of the two medications, each with proven efficacy in treating EPDS, could achieve a more rapid remission. We proposed treating the upper half of the lesion once daily with BDCO and the lower half once daily with tacrolimus 0.1% ointment. A favourable clinical response was observed on both sides of the affected area as early as one week after treatment was initiated. After three weeks of treatment, a satisfactory response was achieved in the BDCO-treated area and a complete clearing of the lesion was achieved in the tacrolimus-treated area *(figure 1B)*. The patient discontinued treatment, with the exception of a small active lesion that was further treated with BDCO three times per week for three months *(figure 1C)* and then until resolution, which occurred after an additional month of treatment. Stable scarring alopecia developed in both halves of the lesion, but there was no recurrence after six months of follow-up. The patient was very satisfied with the efficacy of treatment and had no complaints of inconvenience.

Prompt clinical responses are often noted in patients with EPDS after the application of TCS but such treatment is most often short-lived. To overcome this limitation, several other treatments of EPDS have been attempted, including oral steroids and photodynamic therapy, but have not been consistently effective [6]. Our investigation was undertaken to determine if BDCO was effective in treating EPDS and to determine whether BDCO and tacrolimus differ in the onset of clinical effect or with respect to the frequency of recurrence.

It should be noted that our patient experienced no improvement after many months of systemic treatments before achieving a near-complete recovery in three weeks with tacrolimus and BDCO topical treatments, thus ruling out the occurrence of spontaneous healing. Because we chose a compound such as BDCO, any inference about plain TCS should be made with caution.

Our study suggests that the most remarkable advantage of tacrolimus is the rapidity of healing but patients should be carefully followed to identify any possible neoplastic changes. BDCO has the disadvantage of achieving the same effectiveness as tacrolimus more slowly, albeit with the same low risk for early recurrence despite the significant skin atrophy that developed. BDCO is free of tacrolimus-related concerns regarding skin cancer, apart from the usual careful follow-up required for photo-damaged scalps of elderly patients. ■

Disclosure. *Financial support: none. Conflict of interest: none.*

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doi:10.1684/ejd.2015.2519

Disseminated protothecosis manifesting with multiple, rapidly-progressing skin ulcers: successful treatment with amphotericin B

Protothecosis is a rare infection caused by *Prototheca* species, which are achlorophyllous algae found ubiquitously in nature [1]. Herein, we report a case of disseminated *P. wickerhamii* infection in a patient with systemic lupus erythematosus (SLE). The disease presented as multiple, rapidly-progressing skin ulcers and was successfully treated with systemic antifungal agents.

A 65-year-old Japanese woman was referred to our hospital with a two-week history of extensive ulcerative lesions on the right leg. Physical examination revealed erythematous plaques, nodules and necrotic punched-out ulcers on the leg. The patient suffered from SLE and diabetes mellitus and had been undertaking oral corticosteroid therapy (methylprednisolone, 0.2 mg/kg/day) for 30 years. Because the lesions were refractory to various antibiotic treatments, increased methylprednisolone (0.8 mg/kg/day) was given under the suspicion that the lesions were caused by aggravation of the SLE. However, the lesions worsened and multiple abscesses developed around them. The ulcers rapidly spread over the patient's arms and legs *(figure 1A)*. A skin biopsy specimen showed dense inflammatory infiltrates of neutrophils, lymphocytes and histiocytes in the dermis. Of note, numerous round moruloid bodies of various sizes were scattered in the dermis, suggesting the presence of an infectious microorganism *(figures 1B, C)*. The microorganism was also detected in blood culture when the patient went into septic shock and was isolated as a pure culture on potato dextrose agar. The strain (designated as DMP 14-02) was identified as *P. wickerhamii* by the biochemical sugar assimilation test (API 20C AUX). PCR analyses of its small subunit rDNA, the internal transcribed spacer (ITS) and the large subunit rDNA D1/D2 domain [2] also confirmed the identification. In addition, nucleotide sequencing of the ITS revealed that DMP 14-02 belonged to the genotype 2, similar to the *P. wickerhamii* strains previously isolated in Japan [2]. On the basis of the results of minimum inhibitory concentrations (MICs), we started treatment with intravenous amphotericin B. The skin lesions and vital signs gradually improved after two months of therapy. Amphotericin B was continued for four months and was then changed to oral voriconazole, after which the patient was discharged home.

The current case highlights two important points. First, protothecosis should be included in the differential diagnoses when we encounter rapidly progressing skin ulcers. Protothecosis is often associated with an immunocompromised condition, such as chronic steroid use, diabetes mellitus and organ transplant [1,3,4]. We initially suspected that the patient's skin ulcers were caused by the exacerbation of SLE or SLE-related diseases, including vasculitis, impaired venous circulation and antiphospholipid antibody syndrome. Skin ulcers of these diseases, however, are usually localized and rarely life-threatening. Among six *Prototheca* species, *P. wickerhamii* and *P. zopfii* are common etiological agents in humans, with the former being the most important clinically.

The second point is that the patient was successfully treated with antifungal therapy, mainly using amphotericin B. Protothecosis is classified into three forms in terms of the clinical manifestations, namely, cutaneous (limited to the skin), olecranon bursitis (affecting synovial bursa of the elbow) and disseminated (involving at least two different organs) [4-7]. Todd *et al.* [3] reported that the cutaneous form, of which 75.6% of all *Prototheca* infections consist, has a relatively good prognosis, with a treatment success rate of 73%. In contrast, the disseminated form is rare

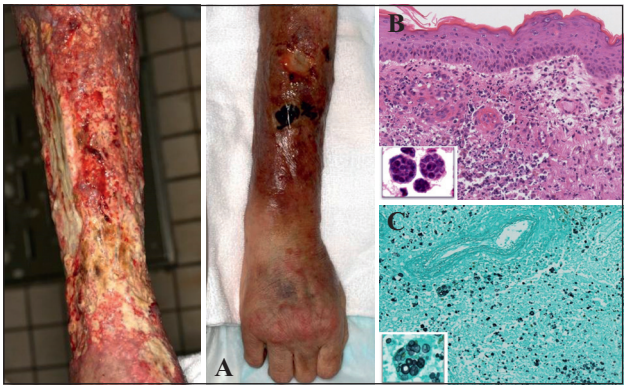

Figure 1. A) Extensive ulcers on the right leg and erythematous plaques with vesiculobullous crust of the right forearm. **B, C)** Numerous round moruloid bodies of various sizes are scattered in the dermis. **B:** hematoxylin and eosin stain, ×40 (inset, ×400); **C**: Grocott's stain, ×40 (inset, ×400).