
Financial Disclosure: None reported.

Funding/Support: This work was supported in part by clinical revenues and generous donors to the Divisions of Dermatology and Dermatopathology, Department of Pathology, Albany Medical College.

1. Fite C, Plantier F, Dupin N, Avril MF, Moyal-Barracco M. Vulvar verruciform xanthoma: ten cases associated with lichen sclerosus, lichen planus, or other conditions. Arch Dermatol. 2011;147(9):1087-1092.

In reply

We appreciate the interest of Carlson et al in our article on vulvar VX1 as well as their comment about the possible etiologic roles of lymphostasis and HPV. Our 10 vulvar VX cases were all associated with another vulvar condition, mainly LS but also lichen planus (2 cases), vulvar radiodermatitis (1 case), and Paget disease (1 case). Our findings sustain the hypothesis of Zegarelli et al that damage to the epithelium—particularly of the DEJ, in our opinion, could trigger the following cascade: (1) entrapment of epithelial cells in the papillary dermis; (2) subsequent degeneration of these cells and lipid formation; (3) engulfment of released lipids by macrophages; and (4) accumulation of foam cells between the rete ridges.

Carlson et al object that this hypothesis does not explain why macrophages accumulate in the papillary dermis. We think that the superficial location of the xanthomatous cells can be explained by the fact that the papillary dermis is the part of the dermis, which is the closest of the damaged epidermis. The poor lymphatic drainage reported by Carlson et al in 14 genital and 4 trunk LS cases could account for the accumulation of macrophages in the papillary dermis. However, to confirm this hypothesis one should demonstrate the following: (1) that all the other conditions associated with mucosal or cutaneous VX are associated with lymphostasis (eg, Paget disease, lichen planus, graft-vs-host disease, discoid lupus erythematosus, pemphigus vulgaris, recessive dystrophic epidermolysis bullosa, lichen planus, epidermal nevus); (2) that lymphostasis is not just an incidental finding related to inflammation, whatever its cause. In addition, if an increased number and dilation of lymphatic vessels is present in most LS cases, these abnormalities cannot alone explain alone the occurrence of VX with LS. Indeed, VX only exceptionally occurs concomitantly with LS.

The second hypothesis advanced by Carlson et al is that the verrucous epidermal hyperplasia that is a hallmark of VX could be related to an HPV infection. This HPV infection may have been facilitated by the lymphostasis, the source of the disrupted immune-cell trafficking and consequently of localized immunosuppression. This interesting assumption is not corroborated either by the pathologic features of VX or by the available virologic data. Indeed, we found that the verrucous hyperplasia of VX had specific, almost pathognomonic, histologic features that differ from those of HPV infections: wedge-shaped parakeratosis forming deep invaginations into the acanthotic epithelium and exhibiting a characteristic orange hue under hematoxylin-eosin stain; and neutrophilic infiltrate at the junction between the superficial parakeratotic layers and the underlying stratum spinulosum. In addition, neither holocytes nor atypia were observed.

In our retrospective study, no HPV search was performed. However, the data collected from the literature are mainly negative, even though very sensitive methods were used.4 A few cases with a positive HPV search have been reported,5 but these findings could have been incidental: HPV may be present on normal vulvar or oral mucosa in as many as 23.3% of the cases.5

Charlotte Fite, MD
Françoise Plantier, MD
Micheline Moyal-Barracco, MD

Author Affiliations: Departments of Dermatology (Drs Fite and Moyal-Barracco) and Pathology (Dr Plantier), Assistance Publique des Hôpitaux de Paris (APHP), Hospital Cochin, Paris Descartes University, Paris, France.

Correspondence: Dr Fite, APHP, Department of Dermatology, 27 rue du Faubourg Saint-Jacques, Paris, 75014 France (Charlotte.fite@noos.fr).

1. Fite C, Plantier F, Dupin N, Avril MF, Moyal-Barracco M. Vulvar verruciform xanthoma: ten cases associated with lichen sclerosus, lichen planus, or other conditions. Arch Dermatol. 2011;147(9):1087-1092.

ONLINE FIRST

Efficacy and Safety of Apremilast in Chronic Cutaneous Sarcoidosis

Pentoxifylline, a phosphodiesterase type 4 inhibitor, is reported to be effective for the treatment of sarcoidosis.1 However, the adverse events associated with this drug have limited its general use. Apremilast is a new phosphodiesterase type 4 inhibitor that blocks the synthesis of proinflammatory cytokines and chemokines, such as tumor necrosis factor, interferon γ, and the interleukins
IL-2, IL-12, and IL-23. These cytokines are important in the initiation and perpetuation of sarcoidosis.

Methods. All the patients included in our trial were required to have active skin lesions consistent with chronic cutaneous sarcoidosis\(^3\) and to be receiving systemic therapy for sarcoidosis that was unchanged for the 3 months before the study entry.

An index lesion was determined at baseline for each patient. For patients with more than 1 skin lesion, the lesion with the highest combined score of induration, erythema, desquamation, and area of involvement was designated the index lesion.

Initially, all patients received oral apremilast, 20 mg, twice a day. If adverse events were reported, the dosage was reduced to 20 mg orally once a day. Patients received 12 weeks of treatment and were seen 1 month later.

Skin lesions were assessed in 2 ways: (1) by using the previously described Sarcoidosis Activity and Severity Index (SASI)\(^3\) and (2) by comparing photographs of the index lesion initially and at week 12, with the photographs presented in random order.\(^3\) The scores were subsequently normalized: 1 indicated much better after therapy and 5, much worse after therapy.

Results. Of 17 patients who provided written consent for participation in the trial, 2 were excluded because of predefined exclusion criteria (1 each for a history of hepatitis C virus and leukopenia). The remaining 15 patients received the drug for the entire study. Individual SASI scores were serially determined by the same investigator for each patient visit in 14 of 15 patients. Apremilast dosage reductions were necessary for 2 patients (1 each for jitteriness and nausea). Both patients completed the study while receiving 20 mg daily without reporting further adverse events.
of the lesions after 4 and 12 weeks of therapy. A significant reduc-
tion in the induration score was noted at both time points
(week 4, $P < .002$; week 12, $P < .005$). Figure 1B demon-
strates the change in induration from baseline for the
index lesion for all 14 patients whose condition was evalu-
ated. Again, we found a significant decrease in the indura-
tion at week 4 ($P < .05$) and week 12 ($P < .02$). Compared
with baseline, there was no statistically significant differ-
ence in the erythema, desquamation, or area of involvement
at week 4 or 12 for all the lesions or for the index lesion.

After 12 weeks of therapy, the normalized mean score
was 2 (“somewhat better after therapy”) for all 3 photo-
graphs. Figure 2 shows a pair of photographs that
were scored by all 3 readers as 1 (“much better after
therapy”). There was good correlation between the dif-
f erent readers (Spearman rank correlation, 0.66-0.81;
$P < .02$ for all 3 correlations).

Within 3 months after discontinuation of apremilast
therapy, 3 patients developed significant worsening of
their cutaneous lesions. In all 3 patients, increasing their
prednisone dosage only moderately improved these lesions.

Comment. To date, there is no consensus regarding the
best method to assess response to therapy for cutaneous
sarcoidosis. The current study used 2 independent in-
struments—the SASI score and paired photographs—to
objectively report changes in cutaneous lesions. The SASI
induration score$^3$ decreased significantly with apremil-
ast therapy (Figure 1). Analysis of paired photographs$^4,5$ also
demonstrated statistically significant improvement. Three patients experienced disease relapse
within 3 months of treatment discontinuation.

We found apremilast effective for some patients who
had persistent lesions despite multiple systemic treat-
ments. This group of patients has been poorly respon-
sive to most other drugs except for high doses of corti-
sosteroids or the anti–tumor necrosis factor antibody
infliximab.$^3$ Further studies seem warranted to examine
the safety and effectiveness of apremilast for the treat-
ment of chronic cutaneous sarcoidosis.

Robert P. Baughman, MD
Marc A. Judson, MD
Rebecca Ingledue, BS
Nico L. Craft, BS
Elyse E. Lower, MD

Accepted for Publication: August 8, 2011.
Published Online: October 17, 2011. doi:10.1001
/archdermatol.2011.301

Author Affiliations: Departments of Medicine, University
of Cincinnati, Cincinnati, Ohio (Drs Baughman and
Lower and Ms Ingledue), and Medical University of South
Carolina, Charleston (Dr Judson and Ms Craft).

Correspondence: Dr Baughman, Department of Medi-
cine, University of Cincinnati, 1001 Holmes, Eden Ave,
Cincinnati, OH 45267 (bob.baughman@uc.edu).

Author Contributions: Drs Baughman, Judson, and Lower
and Ms Ingledue had full access to all the data in the study
and take responsibility for the integrity of the data and
the accuracy of the data analysis. Study concept and de-
design: Baughman, Judson, and Lower. Acquisition of data:
Baughman, Judson, Ingledue, and Craft. Analysis and in-
terpretation of data: Baughman, Judson, and Lower. Draft-
ing of the manuscript: Baughman, Judson, Craft, and Lower.

Critical revision of the manuscript for important intel-
lectual content: Baughman, Judson, Ingledue, Craft, and
Lower. Statistical analysis: Baughman. Obtained funding:
Baughman. Administrative, technical, and material sup-
port: Baughman, Judson, Ingledue, Craft, and Lower. Study
supervision: Baughman, Judson, and Lower.

Financial Disclosure: Drs Baughman, Judson, and Lower
report having acted as consultants to and receiving grants
from Centocor; Drs Baughman and Lower report receiving
grants from Intermune, Actelion, and Cephalon; and
Dr Judson reports receiving grants from Gilead.

Funding/Support: This study was supported in part by
Celgene.

Role of the Sponsors: The sponsor had no role in the
design and conduct of the study; in the collection, analy-
sis, and interpretation of data; or in the preparation, re-
view, or approval of the manuscript.

Trial Registration: clinicaltrials.gov Identifier: NCT00794274

Additional Contributions: Angela Hu, MS, EdM, pro-
vided statistical assistance.

1. Park MK, Fontana JR Jr, Babaali H, et al. Steroid-sparing effects of pentox-
ifyline in pulmonary sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 2009;26

2. Schaler PH, Parton A, Gandhi AK, et al. Apremilast, a CAMP phosphodies-
terase-4 inhibitor, demonstrates anti-inflammatory activity in vitro and in a

cluding lupus pernio: clinical description and proposed scoring systems.

4. Baughman RP, Judson MA, Teirstein AS, Moller DR, Lower EE. Thalidomide

5. Stagaki E, Mountford WK, Lackland DT, Judson MA. The treatment of lupus
468-476.

VIGNETTES

Automobile Seat Heater-Induced
Erythema Ab Igne

E rythema ab igne (EAI), a netlike dermatosis, is
cased by repeated exposure to moderate levels
of heat (infrared radiation). Most seat heaters
reach an upper limit of 43.0°C (109.4°F) with a devia-
tion of about 1.8°C (3.8°F).$^1$ Malfunctioning seat heaters
have reached even higher temperatures, nearing 48.9°C
(120.0°F), causing second-degree burns, especially in pa-
tients with mobility and sensory deficits.$^2$ However, EAI
can occur with chronic exposure to normally function-
ing heated car seats.

Report of a Case. A healthy 40-year-old white woman pre-
vented with a reticular erythematous and hyperpig-
meshed rash restricted to the posterior thighs (Figure 1).

©2012 American Medical Association. All rights reserved.