Role of the Sponsors: The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of data; or in the preparation, review, or approval of the manuscript.

Additional Contributions: Josep Malvehy, MD, helped in the data analysis portion of this study; Narin Apisarnthanarax, MD, helped to recruit and obtain informed consent from patients.


Scalp Dermatomyositis Revisited

A novel study by Kasteler and Callen published in 1994 defined scalp involvement as a common and symptomatic (ie, pruritic) manifestation of dermatomyositis (DM). They defined this involvement as “diffuse, scaly dermatosis with erythema (Figure), atrophy, and often nonscarring alopecia,” present in 82% of their patients with DM. Because therapy to control the often debilitating scalp symptoms of DM is lacking, we conducted a retrospective study to compare the DM cases reported by Kasteler and Callen with our own current population to determine similarities and differences and to evaluate whether any of the systemic therapeutic ladders used to treat DM were optimal for treating symptomatic scalp DM.

Methods. After approval from the institutional review board, we evaluated our patients’ medical charts from 2003 through 2008 that included an International Classification of Diseases, Ninth Revision diagnosis for DM: 24 cases were identified. Diagnosis of DM and scalp DM were based on clinicopathologic correlation by the same observer (J.C.E.). Patient data collected included age, sex, association with alopecia and/or malignant neoplasm, systemic treatment, and clinical outcome. Fifteen patients were noted to have scalp DM, 13 of whom met criteria for treatment analysis (ie, at least 4-month follow-up). We used the Fisher exact test to analyze treatment responsiveness, the clinical endpoints being no relief, partial relief, or complete relief of scalp symptoms from DM.

Results. A comparison of the characteristics of our DM cases with those of the 1994 study is listed in Table 1. Fifteen of our 24 DM cases included scalp involvement, with one-third (n=5) exhibiting associated nonscarring hair loss. All 15 of these patients were women (mean age, 53.3 years), and only 1 had a systemic malignant neoplasm, while 5 had associated myopathy (33%). All 13 patients who met the study criteria received high-potency topical steroid treatment, and only 1 had a partial response. In 11 of the remaining cases, treatment was advanced to the oral immunosuppressive agents listed in Table 2. We observed that 4 of the 11 patients undergoing systemic therapy showed improved cutaneous symptoms but without scalp improvement.

Table 1. Characterization of Patients With Dermatomyositis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Kasteler and Callen,1 1994</th>
<th>Present Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp involvement</td>
<td>14/17 (82)</td>
<td>15/24 (63)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>6/14 (43)</td>
<td>5/15 (33)</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>41.6</td>
<td>55.3</td>
</tr>
<tr>
<td>Associated myopathy</td>
<td>14/14 (100)</td>
<td>5/15 (33)</td>
</tr>
<tr>
<td>Women</td>
<td>13/14 (93)</td>
<td>15/15 (100)</td>
</tr>
<tr>
<td>Malignant neoplasm (Location)</td>
<td>2/17 (12)1b</td>
<td>1/15 (7)</td>
</tr>
</tbody>
</table>

a Unless otherwise indicated, data are reported as number (percentage) of patients.
b Scalp involvement not identified.

Table 2. Summary of Therapeutic Attempts and Improvement in Patients With Dermatomyositis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No Response</th>
<th>Partial Response</th>
<th>Full Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical steroids alone</td>
<td>13</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>5</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>IVIg</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamidea</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviation: IVIg, intravenous immunoglobulins.
a Used as part of breast cancer protocol.
Additional drugs were added to the regimens in some cases if the first treatment attempts failed to improve symptoms. Of 10 patients receiving hydroxychloroquine, none had resolution of scalp symptoms. The progression through the therapeutic ladder (compared with hydroxychloroquine) showed a partial response in 2 of 7 patients treated with methotrexate ($P=.15$) and in 1 of 5 patients treated with mycophenolate mofetil ($P=.33$). The only full resolution of scalp symptoms was seen with intravenous immunoglobulins in a patient for whom all other therapy had previously failed (Table 2).

Comment. Scalp DM presents as a treatment-resistant disease, predominantly in women. Although symptomatic, only 30% to 40% of patients note clinically significant associated alopecia. Amyopathic and/or hypomyopathic DM was more common in our study (66%; $n=10$) than in the 1994 study (100% of patients with muscle involvement [n=14]). In addition, scalp DM seems to have a low association with paraneoplastic DM.

Limitations to our study include its retrospective nature, selection bias in drawing patients from a solely academic practice, and an overall small number of patients.

To our knowledge, no standard therapeutic agents have been used successfully to treat DM with scalp involvement. Although we found no significant difference between systemic agents, treating first with methotrexate or mycophenolate mofetil rather than hydroxychloroquine may be an option for DM when the scalp is involved. A conclusion concerning intravenous immunoglobulins cannot be drawn at this time, but further investigation using a more structured study for treatment of scalp DM is warranted.

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Author Contributions: Dr English had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Prevost, Khera, and English. Analysis and interpretation of data: Tilstra, Prevost, Khera, and English. Drafting of the manuscript: Tilstra, Prevost, and English. Critical revision of the manuscript for important intellectual content: Tilstra, Prevost, Khera, and English. Statistical analysis: Tilstra. Administrative, technical, and material support: Prevost, Khera, and English. Study supervision: Prevost and English.

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COMMENTS AND OPINIONS

Tretinoin: An Established Long-term Safety Profile

We are writing to address the conclusions in the letter “Topical Tretinoin, Lung Cancer, and Lung-Related Mortality” by Katz. The Veterans Affairs Topical Tretinoin Chemoprevention (VATTC) trial was a double-blind study conducted to assess the value of tretinoin, 0.1%, cream in the prevention of nonmelanoma skin cancer. Katz concludes that while it is not clear whether tretinoin caused the excess lung-related deaths in VATTC, concern was warranted because a causal link was plausible. Results presented by Weinstock et al reveal minor imbalances in morbidity predictors such as age, comorbidities, and smoking status, and the authors conclude that a causal relationship between topical tretinoin therapy and death cannot be inferred. Thus, the supposition by Katz is in clear contrast to the conclusions of Weinstock et al.

Katz also suggests that individuals who rapidly metabolize tretinoin are more susceptible to developing non–small cell lung cancer and cites a study by Rigas et al of the metabolism of orally administered all-trans retinoic acid (ATRA) in healthy subjects and subjects with lung cancer. However, Rigas et al found that if ATRA is critical to normal expression of retinoic acid receptor $\beta$, then a rapid catabolic phenotype might account for accelerated oxidative activity that results in decreased nuclear ATRA levels. Rigas et al also reference studies indicating that retinoid supplements have proven most effective in the treatment and prevention of smoking-related premalignant or squamous cell cancers of the lung, head, and neck. Finally, Rigas et al conclude that diminished levels of ATRA and metabolites might result in an increased susceptibility to carcinogenesis and that high levels of ATRA might prevent cells from escaping normal growth controls and progressing to neoplasia after carcinogenic exposure.

Katz also implicates tretinoin as a disease-causing agent based on data from studies of beta carotene, a vitamin A precursor. However, published studies that have linked lung cancer incidence in smokers with beta carotene levels have attributed the effect to high doses of oral beta carotene alone, not its metabolites. There are numerous examples of prooxidant activity by beta carotene. Beta carotene may act as a prooxidant under conditions such as those seen in smokers. The beta carotene radical is a strong oxidizing agent and, depending on the microenvironment, may have a long lifetime, which could explain the procarcinogenic effect of beta carotene in smokers. Thus, the association between beta carotene and lung cancer is independent of the formation of vitamin A and/or its metabolites and therefore not relevant to tretinoin.

The safety of tretinoin has been clearly established through a battery of clinical and toxicologic studies. Long-term clinical studies in humans (up to 2 years) have been conducted without report of severe adverse events or safety...