

**RESEARCH LETTER**

**Association of Topical Corticosteroids With Reduced Vulvar Squamous Cell Carcinoma Recurrence in Patients With Vulvar Lichen Sclerosis**

Vulvar lichen sclerosus (vLS), if untreated, results in a 5% to 7% increased lifetime incidence of vulvar squamous cell carcinoma (vSCC) and differentiated vulvar intraepithelial neoplasia (dVIN). This incidence rate can be reduced by suppressive topical corticosteroid treatment; however, whether topical corticosteroid therapy can also reduce the rate of vSCC recurrence remains unknown. Current data report a 5-year rate of recurrence of 44% to 47% after surgical treatment. Furthermore, if a patient had 1 recurrence, their chance of another recurrence within 5 years rises to 80%. Determining whether topical corticosteroid treatment after surgery can reduce the risk of recurrence is important because up to 25% of women with vLS report not being treated with topical corticosteroid after vSCC excision. If shown to have an association with preventing cancer recurrence, topical corticosteroid therapy could be readily implemented.

**Methods** | The recurrence rate of vSCC or dVIN in patients with vLS who received long-term topical corticosteroid therapy was investigated through a medical record review of a dermatogynecology practice in Sydney, Australia. The computerized database, presently containing 2410 patients with vLS, was set up in 2008 to undertake a prospective cohort study of vLS, and patients remain under surveillance. The study was approved by the ethics committee of North Shore Private Hospital in Sydney, Australia, and written informed consent was obtained from all participants. All patients were treated with topical corticosteroids after primary excision of vSCC or dVIN. Agents used included betamethasone dipropionate, 0.05%, methylprednisolone aceponate, 0.1%, hydrocortisone, 1%, clobetasol propionate, 0.02% and 0.05%, and desonide, 0.05%. These agents were prescribed for daily application and titrated to a desired outcome of disease suppression, which was defined as skin of normal texture with loss of white discoloration. Patients were followed up at intervals of 3 to 12 months and were asked about adherence to the drug regimen using a 5-point Likert scale from 0 (not at all) to 5 (every specified day). Adherence was defined as a score of 4 (most days) or 5 (every specified day). Recurrence was defined as new dVIN or vSCC in a region of tissue where dVIN or vSCC had been previously excised with clear margins.

**Results** | From January 1, 2008, to April 30, 2019, the medical records of 25 patients with vLS and previous vSCC and/or dVIN were reviewed. Ten patients with human papillomavirus (HPV)-associated dVIN or HPV-associated vSCC were excluded. Ten patients with human papillomavirus (HPV)-associated dVIN or HPV-associated vSCC were excluded. The

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**Table. Recurrence of vSCC or dVIN in Patients With Vulvar Lichen Sclerosis Who Were Treated and Adhered to Topical Corticosteroid Therapy**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age range at diagnosis of primary lesion, y</th>
<th>Primary lesion (vSCC/dVIN)</th>
<th>P16 result/formal HPV result*</th>
<th>Initial management of primary lesion</th>
<th>Surgical margins</th>
<th>Recurrence</th>
<th>Time to recurrence, mo</th>
<th>First</th>
<th>Second</th>
<th>Follow-up time, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50-60</td>
<td>vSCC and dVIN</td>
<td>Negative/NA</td>
<td>Surgical excision with node dissection</td>
<td>Clear</td>
<td>No</td>
<td>NA</td>
<td>14</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>60-70</td>
<td>vSCC and dVIN</td>
<td>Negative/negative</td>
<td>Surgical excision</td>
<td>Clear</td>
<td>Yes</td>
<td>16 (dVIN)</td>
<td>NA</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>70-80</td>
<td>vSCC</td>
<td>Negative/NA</td>
<td>Surgical excision with node biopsy</td>
<td>Clear</td>
<td>No</td>
<td>NA</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>60-70</td>
<td>vSCC</td>
<td>Negative/NA</td>
<td>Surgical excision with node dissection</td>
<td>Clear</td>
<td>No</td>
<td>NA</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>80-90</td>
<td>vSCC</td>
<td>Negative/NA</td>
<td>Surgical excision with node dissection</td>
<td>Clear</td>
<td>No</td>
<td>NA</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>70-80</td>
<td>vSCC</td>
<td>Negative/NA</td>
<td>Surgical excision</td>
<td>Clear</td>
<td>Yes</td>
<td>27 (vSCC)</td>
<td>NA</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>50-60</td>
<td>vSCC</td>
<td>Negative/NA</td>
<td>Surgical excision with node dissection</td>
<td>Clear</td>
<td>Yes</td>
<td>103 (dVIN and vSCC)</td>
<td>132 (vSCC)</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>50-60</td>
<td>dVIN</td>
<td>Negative/NA</td>
<td>Surgical excision</td>
<td>Clear</td>
<td>No</td>
<td>NA</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>20-30</td>
<td>dVIN</td>
<td>Negative/NA</td>
<td>Surgical excision</td>
<td>Clear</td>
<td>No</td>
<td>NA</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>70-80</td>
<td>vSCC and dVIN</td>
<td>Negative/negative</td>
<td>Surgical excision with laser therapy</td>
<td>Initially incomplete, proceeded to further excision (clear margins achieved) with node biopsy confirmation</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>60-70</td>
<td>dVIN</td>
<td>Negative/negative</td>
<td>Surgical excision with laser therapy</td>
<td>Clear</td>
<td>No</td>
<td>NA</td>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: dVIN, differentiated vulvar intraepithelial neoplasia; HPV, human papillomavirus; NA, not applicable; vSCC, vulvar squamous cell carcinoma.

* P16 is a surrogate marker of human papillomavirus.
cluded. One patient who did not adhere to topical corticosteroid therapy and 3 patients with less than 5 years of follow-up (or loss to follow-up) were excluded. In the remaining 11 patients, mean age at diagnosis of primary lesion was 62.9 years (range, 26-88 years). Initial management of vSCC or dVIN included surgical excision alone in 4 patients, surgical excision with node biopsy in 2 patients, surgical excision with node dissection in 4 patients, and surgical excision with adjuvant laser therapy in 1 patient. Of 11 patients, 8 (73%) remained free of recurrence with a mean follow-up of 10.5 years (range, 5.1-16.5 years) (Table). Two patients (18%) had recurrence of their vSCC, 1 of whom developed multiple recurrences of vSCC, and 1 patient (9%) had recurrence of their dVIN.

Discussion | In the study cohort, patients with vLS who adhered to topical corticosteroid therapy had a vSCC or VIN recurrence rate of 27% compared with reported 5-year recurrence rates of 44% to 47%.4,5 Only 1 patient with a recurrence of vSCC or dVIN had a subsequent recurrence compared with the 5-year subsequent recurrence rate of 80% for untreated vLS. It has been hypothesized that chronic inflammation contributes to the increased risk of developing vSCC; thus, the anti-inflammatory effect of topical corticosteroid may confer a protective benefit.6 Topical corticosteroid treatment is inexpensive and safe and could result in considerable cost savings and reductions in morbidity and mortality.

A limitation of the present study is that it is a single-center retrospective medical record review with a small sample size; there was no control group (patients not treated with a topical corticosteroid) for comparison. A strength of the study is that all included patients were part of a large cohort with vLS who have been followed up prospectively since 2008. Larger prospective studies including a control group for comparison would strengthen the evidence of the findings in this report.

Topical corticosteroid therapy may represent an important management strategy to reduce the recurrence rate of vSCC and dVIN in patients with vLS. These findings suggest the need for a large prospective trial. However, in the meantime, we encourage dermatologists to play an active role in assisting colleagues who specialize in gynecology-oncology to use a topical corticosteroid when treating patients with vLS.

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Author Contributions: Drs Lee and Fischer are considered coauthors and contributed equally to this work. Drs Chin and Fischer 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.

Concept and design: Scurry, Bradford, Lee, Fischer.
Acquisition, analysis, or interpretation of data: Chin, Lee, Fischer.
Drafting of the manuscript: Chin, Lee, Fischer.
Critical revision of the manuscript for important intellectual content: Scurry, Bradford, Lee, Fischer.
Statistical analysis: Chin, Lee.
Administrative, technical, or material support: Lee.
Supervision: Lee, Fischer.

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Calcinosis Cutis in the Setting of Chronic Skin Graft-Versus-Host Disease

Calcinosis cutis is a recognized sequela of systemic sclerosis (SS).1 Systemic sclerosis and sclerotic-type chronic skin graft-versus-host disease (ScGVHD) share several clinical and histologic features; however, high-titer antibodies specifically associated with SS are not typically found in ScGVHD, and the fibrotic features in ScGVHD more closely resemble morphea and eosinophilic fasciitis.2 Whereas calcinosis is well described in SS, there are only 2 reports of calcinosis in the setting of chronic graft-versus-host disease (cGVHD), to our knowledge.3,4 We sought to identify patients with cGVHD with calcinosis to explore predisposing factors and clinical features.

Methods | We identified 7 patients with GVHD-associated calcinosis cutis (GVHD-CC) from 3 academic dermatology programs. Data were collected retrospectively from medical chart review. Patients evaluated at the National Institutes of Health were evaluated under a research protocol (04-C-0281) approved by the National Institutes of Health institutional review board. The institutional review board of the University of Pennsylvania and Washington University School of Medicine at St Louis did not require institutional review board approval for the contribution of single cases. The deidentified data are presented as a retrospective case series collected from 2014 to 2018.

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