Is Vulval Erosive Lichen Planus a Premalignant Condition?

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Clinical Question: What is the evidence for erosive lichen planus affecting the vulva being a premalignant condition?

Background

A 58-year-old woman presented to the Vulval Dermatology Clinic with a 4-month history of vulval burning and irritation. Her quality of life was significantly affected: she reported pain while urinating, was unable to wear certain clothing, and experienced dyspareunia. Treatment for thrush using over-the-counter medications had resulted in worsening symptoms.

Examination showed tender erythematous erosions with a white border, located at the vaginal introitus. These lesions were tender. Inspection of the oral cavity revealed bilateral lacy white plaques on the buccal mucosa. The oral lesions were asymptomatic. Biopsy from the edge of a vulval erosion was in keeping with the clinical diagnosis of erosive lichen planus.

The patient was counseled about the possible risk of squamous cell carcinoma (SCC) of the vulva, which is associated with the condition. She asked about the magnitude of that risk, but we were unable to give an exact figure. This prompted our review of the literature.

Erosive lichen planus is an uncommon, chronic inflammatory condition mainly affecting the mucosal surfaces of the mouth and genitalia. It is thought to be an autoimmune disorder with T cell–mediated damage to basal keratinocytes.1,2 Vulval erosive lichen planus (ELPV) causes painful erosions and scarring of the vulva and vagina. Some researchers have postulated on the basis of case reports3–5 that ELPV lesions may develop into SCC.3 However, ELPV is underresearched and evidence from larger-scale studies is lacking. This critically appraised topic6 aims to evaluate the evidence to determine whether ELPV is associated with an increased risk of vulval SCC.

Literature Search

We searched the MEDLINE, EMBASE, and Cochrane Library databases on December 7, 2011. The MEDLINE search strategy is illustrated in the Figure. No restrictions were imposed regarding the publication date, although articles were restricted to those in the English language. Overlap diagnoses of lichen sclerosus and lichen planus were excluded. Because case reports are subject to reporting bias and had the potential to skew our overall conclusion toward a positive association, we restricted our search to case series involving 5 or more consecutive patients with ELPV seen in a specialist clinic. The search strategy retrieved 142 articles. Of this number, 42 articles were selected for detailed review.

We identified 4 case series7–10 that described the long-term follow-up of a total of 366 patients with ELPV. In addition, 2 case series11,12 of patients with anogenital carcinoma were found in which the authors investigated the underlying etiology of the malignancy. Five case reports13–15 that described SCC occurring in association with ELPV (in a total of 6 patients) were also found; however, these were excluded.

Appraisal of the Evidence

Combining findings from the 4 case series, vulval SCC occurred in 5 of 366 patients. The overall duration of ELPV was reported for only 1 of these incident cases (3 years).9 Mean follow-up time was documented by only 2 studies (606 and 725 months). Three studies were retrospective and 1 was prospective. These are summarized in the Table.

Santegoets et al17 performed a retrospective clinical study using medical records from 95 patients who pre-
sent to a single vulval outpatient clinic in the Netherlands. Vulval SCC developed during follow-up in 2 patients. No further information was provided on duration of disease, age, response to treatment, or outcome following surgery for SCC.

Kennedy et al\(^\text{10}\) reported a retrospective series of 113 patients who had presented to a specialty clinic with a new diagnosis of ELPV. Their primary aim was to assess the occurrence of cancer (of any type) in the patient cohort. Average follow-up for the entire cohort was stated as 5 years, although it is unclear whether this is the mean value and the range was not given. One patient developed vulval SCC 3 years after her diagnosis of ELPV. However, this was a relatively young patient (aged 40 years) who had received chemoradiotherapy 1 year earlier for likely human papillomavirus (HPV)–related cervical cancer. She also was relatively immunosuppressed secondary to medical comorbidities (Table). In this series, a different patient developed oral SCC and another developed esophageal SCC. These patients had an underlying diagnosis of oral erosive lichen planus. Other seemingly unrelated malignant tumors also occurred within this cohort (Table).

Kirtschig et al\(^\text{12}\) retrospectively assessed the medical records of 44 patients. The mean follow-up was not stated. One patient developed vulval SCC 18 months after her first vulval symptoms. There was no comment about age of onset, severity, response to treatment of ELPV, comorbidities, or outcome following SCC treatment for this patient.

The only prospective cohort study identified was by Cooper and Wojnarowska,\(^{8}\) who followed up 114 patients for a mean of 72 months. Vulval intraepithelial neoplasia preceded the development of vulval SCC in 1 patient. Squamous cell carcinoma occurred in another 2 patients, but the site affected was the perianal location in 1 and the oral location in 1. It was implied, although this was not explicitly stated, that both of these sites were affected by erosive lichen planus before the development of malignancy. Vulval intraepithelial neoplasia occurred in another 6 patients. There was no comment on HPV status, comorbidities, the duration or severity of disease, or the response to treatment in the affected individuals. The prevalence of SCC development (any site) for this cohort was calculated at 3% during 72 months.

Of the 2 series that reviewed cases of anogenital carcinoma and investigated the underlying etiology, ELPV was implicated histologically in 6 of 84 occurrences of SCC. One study\(^\text{11}\) identified 61 cases of vulval SCC from the histology department of a tertiary referral center and examined the adjacent epithelia for associated skin conditions. Eleven samples were excluded because adjacent epithelium was not present in the specimens. Epithelial disease was present in 40 of the 50 remaining specimens, 3 of which showed lichen planus. The sec-

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**Table. Summary of Case Series Included in Critically Appraised Topics**

<table>
<thead>
<tr>
<th>Source</th>
<th>Study Type</th>
<th>Study Period</th>
<th>No. of Patients</th>
<th>Diagnostic Criteria for ELPV</th>
<th>Mean Follow-up, mo</th>
<th>No. of Patients With Malignant Tumor (Duration of Preceding ELPV if Known)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Santegoets et al(^\text{7})</td>
<td>Retrospective case series (C)</td>
<td>May 1995–Dec 2002</td>
<td>95</td>
<td>Single experienced physician looking for sharply demarcated erythema at vestibule, with or without WS, sharply demarcated erosions of vaginal wall, and involvement of other sites</td>
<td>Unknown</td>
<td>2 (Unclear)</td>
</tr>
<tr>
<td>Kennedy et al(^\text{7})</td>
<td>Retrospective case series (C)</td>
<td>Jan 1995–Dec 2002</td>
<td>113</td>
<td>Single experienced physician looking for WS on mucous membranes and microscopy showing inflammatory cells</td>
<td>Biopsy only if clinical diagnosis unclear (number performed not stated)</td>
<td>60</td>
</tr>
<tr>
<td>Cooper and Wojnarowska(^\text{8})</td>
<td>Prospective cohort study (B)</td>
<td>5-y period, unclear timeline</td>
<td>114</td>
<td>“Definite” clinical diagnosis (criteria not specified)</td>
<td>Biopsy only if clinical diagnosis unclear (performed in 97 of 114 patients); histologic samples graded as diagnostic, probable, possible, nondiagnostic; absence of biopsy findings was not a contraindication to inclusion if classical clinical features were exhibited</td>
<td>72</td>
</tr>
<tr>
<td>Kirtschig et al(^\text{10})</td>
<td>Retrospective case series (C)</td>
<td>1997–2000</td>
<td>44</td>
<td>Clinical diagnosis of ELPV (criteria not specified)</td>
<td>Biopsy performed in 38 of 44 patients (6 declined); histologic samples defined as diagnostic, consistent, nonspecific</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Abbreviations: adenoca, adenocarcinoma; ELPV, vulval erosive lichen planus; SCC, squamous cell carcinoma; VIN, vulval intraepithelial neoplasia; WS, Wickham striae.

\(^{8}\) As described by Robinson et al.\(^{16}\)
ond study\(^2\) retrospectively analyzed the presence of coexisting skin disease in 21 women with vulval SCC. Clinical features of ELPV were present in 3 and histologic features were present in 4 of these patients. In these 2 studies, the vulval condition most commonly associated with SCC was, as expected, lichen sclerosus.

**Limitations of the Critically Appraised Topic**

The true incidence of ELPV is difficult to assess because patients present to a number of different specialists for treatment. Furthermore, unless an examining physician specifically asks, vulval disease may go undiagnosed in a patient who presents with lichen planus elsewhere. Few studies have been performed to characterize the natural history of ELPV and, to our knowledge, no randomized controlled trials to provide evidence for treatment have been published.\(^3\)

Only one of the studies that we identified had explicitly set out to determine the occurrence of cancer in patients with ELPV.\(^4\) The remainder aimed to study clinical and histopathologic features and the response to treatment of the disease; assessing the development of malignant tumors was not their primary aim. Furthermore, only 1 study had been performed prospectively.\(^5\) This could explain why certain information that would usually be included when reporting the development of malignant tumors in a cohort study (eg, follow-up period) was not available and we were therefore unable to calculate prevalence rates.

Although a description of how the clinical diagnosis was made was present in 2 articles,\(^6\) it was not in the others. Specimens for histologic examination were not collected from all patients, and therefore we cannot be certain that all patients who developed SCC had a definite initial diagnosis of ELPV (although it is likely because all investigators were experts in their field).

Finally, except for the 1 patient reported by Kennedy et al,\(^7\) there were no data offered regarding the possibility of latent infection with HPV in the patients who developed SCC. Because HPV is an important etiologic factor in the development of anogenital intraepithelial neoplasia (and subsequent frank malignant tumor), it would be useful to gather data about HPV status in patients with ELPV in future prospective studies.

**Clinical Bottom Line**

The incidence of vulval carcinoma varies from less than 1 in 100,000 women in developing countries to more than 1.5 in 100,000 women in North America, South America, and Europe.\(^8\) Insufficient data are present from the identified case series to calculate the incidence and prevalence of SCC within the population with ELPV. There is clear evidence that certain vulval inflammatory disorders, such as lichen sclerosus,\(^9\) predispose to the development of malignancy. Although there is a suggestion of an increased prevalence of vulval SCC in patients with ELPV, the only way to clarify this is for long-term follow-up data of the disease and its complications to be recorded in a multicenter registry.

**What Happened to Our Patient?**

Following a reducing regimen of topical clobetasol propionate, 0.05%, our patient currently has adequate control of her disease with improved symptoms and function. She will continue with follow-up on a 3- to 6-month basis depending on the level of disease control. She has been educated about the importance of self-examination between clinic appointments to monitor for the development of malignant tumors. Given our current understanding, her follow-up will be long term owing to the perceived increased risk of developing SCC of the vulva associated with the ELPV.

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**REFERENCES**