# BRIEF ARTICLES

## Hypertrophic Lichen Planus versus Well-Differentiated Squamous Cell Carcinoma: A Histological Challenge

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### ABSTRACT

Differentiating hypertrophic lichen planus (LP) from well-differentiated squamous cell carcinoma (SCC) is a histological challenge given the numerous histopathologic similarities between SCC and pseudoepitheliomatous hyperplasia (PEH) arising in the setting of hypertrophic LP. Multiple reports have shown that SCC can arise from hypertrophic LP not infrequently, but that the LP-to-SCC sequence is poorly understood, and many cases defy diagnosis due to histologic similarities. However, there are several clinical clues and histopathologic details that have shown to have some value when trying to ascertain the correct diagnosis. To the contrary, immunohistochemical tests have shown little promise in differentiating hypertrophic LP from SCC. Although multiplex PCR has shown some potential in differentiating PEH from SCC, this has only been in the setting of patients diagnosed with prurigo and lichen simplex chronicus, but not necessarily in the case hypertrophic LP.

### CASE DESCRIPTIONS

A 74-year-old woman presented with a 3 month history of an itchy rash on the dorsal forearms and left anterior shin. Physical exam revealed violaceous scaly papules and plaques along the dorsal forearms, as well as a hyperpigmented verrucous plaque with nodules along the left anterior shin (figure 1). Initial biopsy of the left anterior shin revealed well-differentiated squamous cell carcinoma (SCC, figure 2); however, due to a clinical appearance consistent with hypertrophic lichen planus (LP), three more biopsies were taken. Two of these were read as hypertrophic LP, while the third was analyzed as a non-specific squamous proliferation. The initial biopsy was subsequently re-classified as pseudoepitheliomatous hyperplasia (PEH), and the patient was diagnosed with hypertrophic LP and underwent improvement with clobetasol and kenalog treatment.

A 55-year-old female on hemodialysis for chronic kidney disease presented with a 7 month history of an itchy rash on the extremities and back. Physical exam revealed many excoriated papules and nodules along with some lichenified, flat-topped papules throughout all of these

areas. Additionally, three 1.3-1.5 centimeter pink nodules were noted on the lower legs (figure 3). Biopsies of the nodules were taken, and although the patient's clinical appearance was consistent with hypertrophic LP, the nodules were diagnosed as well-differentiated SCC's, and were treated as such.

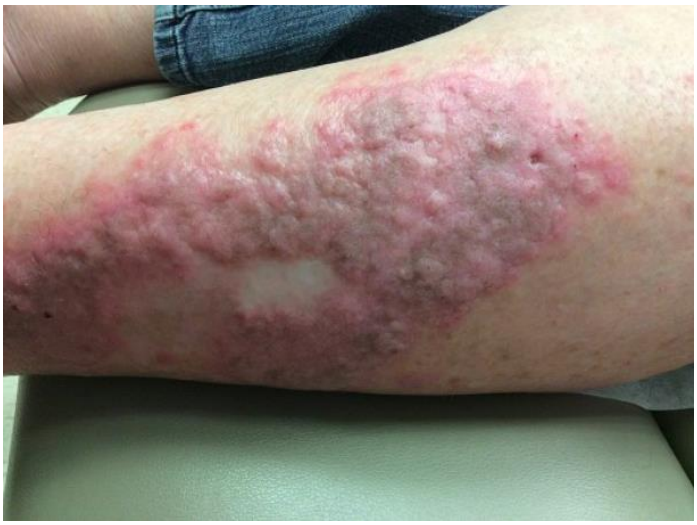

FIGURE 1: Hyperpigmented verrucous plaque with nodules along the left anterior shin, suspicious for hypertriphic lichen planus.

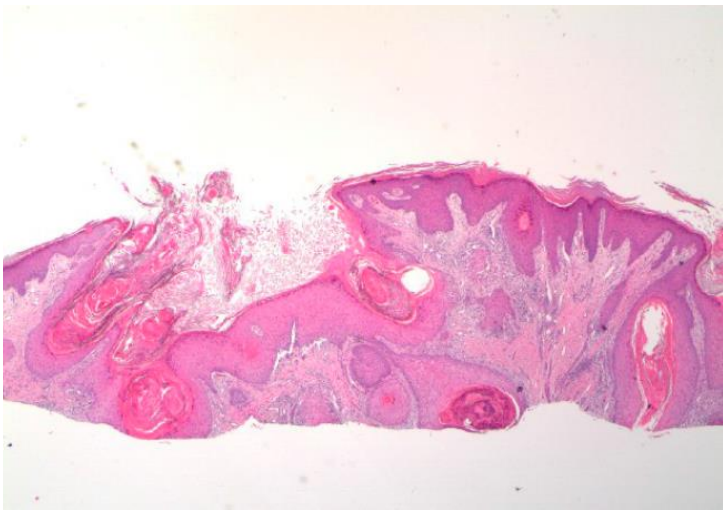

FIGURE 2: Biopsy of the above lesion was initially read as well-differentiated squamous cell carcinoma, but the diagnosis was revised to pseudoepitheliomatous hyperplasia arising in the presence of hypertrophic lichen planus upon clinical review and additional biopsies.

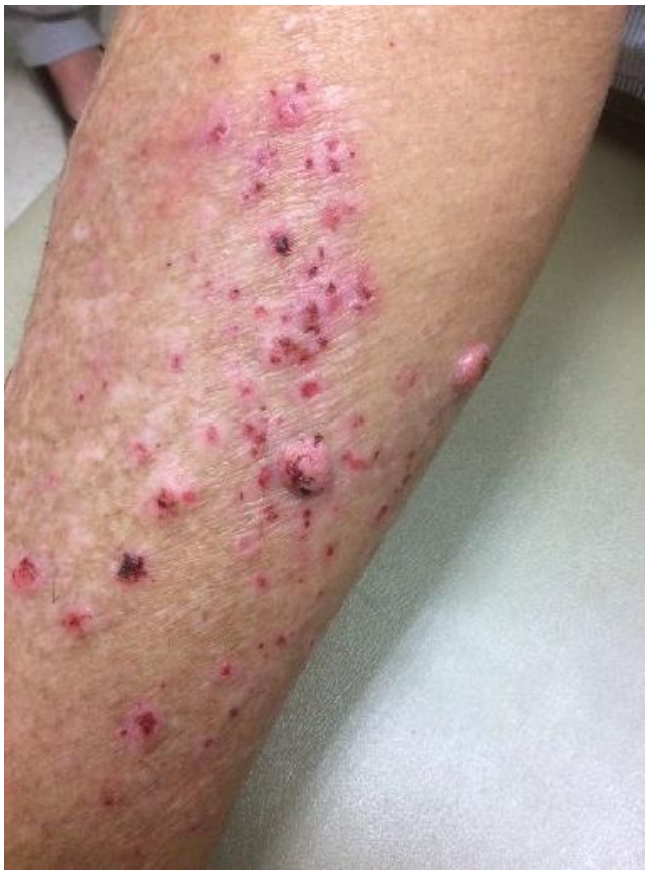

FIGURE 3: Nodules suspicious for squamous cell carcinoma arising in the setting of hypertrophic lichen planus.

## DISCUSSION

Ninety-one total cases of the LP-to-SCC transition have been reported, and over 50 of them have occurred in the context of hypertrophic LP[1]. Features unique to the growth of SCC in the context of LP include that the lesions tend to present below the knee, are more frequent in male patients, and the average age is older than 55[2]. Likewise, authors have reported a 0.4% incidence of malignancy for cutaneous LP, and noted that chronicity is a risk factor for malignant transformation, as the typical LP patient is afflicted for more than 11 years before malignancies tend to develop.

Similarly, multiple studies have commented on the difficulty of differentiating SCC from PEH arising from hypertrophic LP histologically, and a multitude of prior cases have been reported in which the preliminary diagnosis of SCC was reversed to hypertrophic LP following supportive clinical evidence[1,3]. In the majority of these cases the lesions showed significant improvement with near-resolution by 6 months following treatment with topical steroids[1]. Likewise, in each of these cases the histologic diagnosis was reversed from SCC to PEH, which can be the result of many different chronic inflammatory processes and is characterized by gross acanthosis, moderate dyskeratosis, and downward proliferation with horn cysts on histology. However, in PEH, lymphovascular and perineural invasion is absent, and there is no inclusion of the deep dermis.

Identifying SCC's in the context of hypertrophic LP has been a common difficulty since the LP-to-SCC sequence is poorly understood histologically; as such, many cases of SCC arising in hypertrophic LP may not initially be accepted as such[4]. However, it is equally easy to misidentify PEH as SCC, particularly in the context of superficial shave biopsies. Histologic clues that may differentiate hypertrophic LP from SCC include the presence of a lichenoid infiltrate at the tips of the rete ridges along with dyskeratosis, pigment incontinence, and lack of cytologic atypia[5]. However, since PEH can present with "irregular strands, cords, and nests of squamoid cells extending into the dermis" along with "substantial nuclear atypia and mitoses," some cases can simply "defy definitive classification"[6].

In regards to immunohistochemistry, P53 expression is seen in all cases of PEH and 75% of SCC cases, although the staining pattern is less intense and extensive in PEH as compared to SCC[4]. Additionally, both stain similarly to proliferating cell nuclear antigen, and although E-cadherin has been reported to be lost in SCC but preserved in PEH, it has been found to stain both PEH and SCC samples equally. Furthermore, although there are decreased Langerhans cells compared to normal epidermis in PEH, SCC also has reduced numbers of CD1-a positive cells. Although P63 was used for one case to distinguish PEH from SCC in the case of a granular cell tumor of the tongue, it has not yet been used for LP[7]. Lastly, Ki-67 has been found to be present in the basal layer of both PEH and SCC[4]. Due to the lack of immunohistochemical differences, it has been suggested that the presence of multiple lesions, clinical follow-up, and proliferation from follicular infundibula are the most reliable markers to point towards PEH rather than SCC.

To address the problem that there have not been immunohistochemical or molecular tests to date to differentiate SCC from PEH, multiplex PCR was tested and shown to differentiate cutaneous SCC from PEH in 53 of 58 cases (93%)[6]. The genes *C15orf48*

and *KRT9* have been found to have distinct gene expression patterns in SCC and PEH, with *C15orf48* having a higher expression than *KRT9* in SCC, but lower in PEH. However, in the aforementioned research, the PEH cases were selected from patients diagnosed with prurigo or lichen simplex chronicus, so the generalizability of the study to the case of PEH arising in the setting of cutaneous LP is unknown.

In summary, transition from cutaneous LP to SCC is somewhat rare, with less than 100 reported cases in total, but over half of these cases have arisen in the context of hypertrophic LP[1]. Many cases of SCC may be missed since there is not a well-known cutaneous LP-to-SCC histologic sequence, but it is very difficult to differentiate SCC from PEH arising in the context of hypertrophic LP, and many cases may lie in a "grey zone" due to histologic similarities[4]. However, histologic clues that point to PEH include a lichenoid infiltrate at the tips of the rete ridges along with dyskeratosis, pigment incontinence, lack of cytologic atypia, and proliferation from follicular infundibula[4,5]. Furthermore, clinical clues such as response to steroids and multiplicity and acuity of lesions may be more useful than histopathology to indicate PEH rather than SCC[1,3,4].

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