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Clinical Decision Making Based on Histopathologic Grading and Margin Status of Dysplastic Nevi

The purpose of the present study was to determine how clinicians elect to treat a histologic dysplastic nevus (DN) given a reported grade of the dysplasia and margin involvement on a biopsy report.

Methods. An anonymous survey was distributed to the members of the Chicago Dermatologic Society during the annual meeting in March of 2009. Respondents were asked what clinical decisions they would make based on hypothetical pathology reports of varying histopathologic grades of DN with and without margin involvement. For survey purposes, we characterized DN as histopathologically displaying mild, moderate, or severe atypia. We did not specify if the nevi were primarily graded on the architectural or cytologic features. A total of 6 case scenarios were presented to the respondents. The survey questions were presented as follows:

Biopsy report states the patient has a mildly (or moderately/severely) dysplastic nevus with positive (or clear) margins. Elect to: Observe, Re-excise or Other.

A freehand response was allowed for the "Other" option. Institutional review board approval was waived for this anonymous survey.

Results. Of the 158 surveys distributed, 101 were returned for a 58% response rate. There was no significant difference in the probability of electing to reexcise nevi with mild vs moderate dysplasia in patients with clear margins reported on pathologic evaluation (Figure, A). If the margins were positive, there was a significantly greater probability of electing to reexcise the DN for all grades of dysplasia (Figure, B). The greatest quantitative shift in decision making (from observe to reexcise) as a function of involved margins was seen for DN with moderate dysplasia. Specifically, the decision to reexcise DN with moderate dysplasia inverted from 9% to 81% of respondents.

Comment. This study finds that both grade and margin status are important variables in determining surgical decisions; margin status is most influential when applied to DN of moderate grade. Margin status does not appear to be as critical for clinical decision making of DN with mild or severe dysplasia.

Previous studies,^{1,2} also using surveys, have attempted to elicit the reexcision rate of DN histologically confirmed, but those studies did not directly address the histologic grade of the lesion or the margin status of the biopsy specimen. The responses from both of those studies indicated that both the margin status and the degree

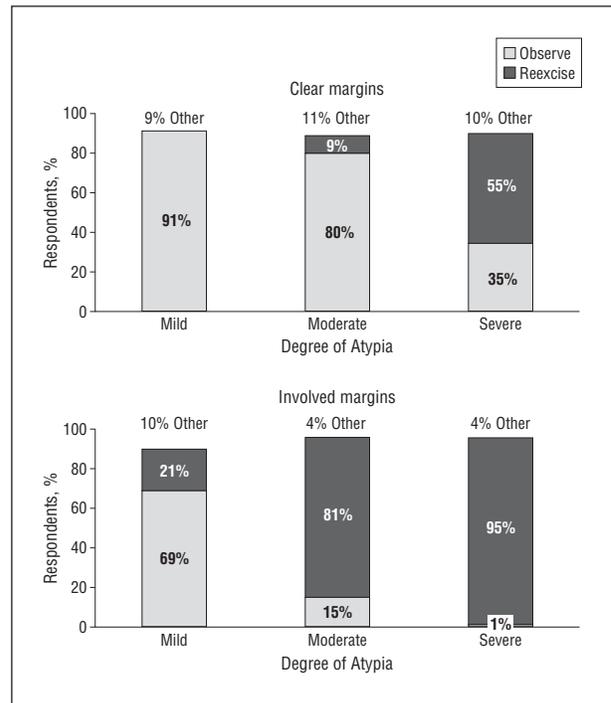


Figure. Degree of atypia with clear margins (A) and involved margins (B).

of dysplasia had some role in the decision to reexcise. The present study addresses the effect of both degree of atypia and margin status reported on the clinician's decision to observe or reexcise a DN.

The DN is a controversial subject in dermatology, and although there are no universally accepted criteria for grading DN (or the biologic consequence of these lesions), it remains common clinical practice. In our small sample, 83% of respondents indicated that the dermatopathology reports they receive comment on the grade of a dysplastic nevus.

Our findings are relevant because there is mounting evidence that reexcision of lesions with low-grade atypia (mild and moderate DN) may not be necessary, even when positive margins are found^{3,4}; the recurrence rates of these nevi are low, and there are no reports of subsequent development of melanoma in these lesions. Larger prospective trials are still needed to help define a standard of care with respect to histopathologically proven DN.

Our survey demonstrates the likely clinical decisions given a pathology report defining the degree of histopathologic atypia and margin involvement. It is helpful for dermatopathologists to know the clinical consequences of their pathology report and for other clinicians to see how their colleagues approach these controversial lesions.

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Lichen Sclerosus Exhibiting Histologic Signs of Lymphedema: An Essential Factor in the Pathogenesis of Verruciform Xanthoma

Recently, Fite et al¹ reported a series of vulvar verruciform xanthomas (VX) and attributed VX pathogenesis to disorders that injure the dermoepidermal junction (DEJ), namely lichen sclerosus (LS). While we agree that damage to the DEJ is the source of debris found in the xanthomatous macrophages of VX, the LS theory does not explain the accumulation of lipophages in the papillary dermis or the superimposition of verrucous epidermal hyperplasia—the 2 pathognomonic features of VX.

Our research group² has recently reported evidence that VX is a complication of localized lymphedema, which has many causes, including trauma, surgery, radiation therapy, neoplasia, infection, and inflammatory dermatoses.³ Specifically, scarring due to trauma, repeated irritation, and/or chronic inflammation can obstruct lymphatics and lead to lymphostasis, histologically denoted by lymphangiectases. Regional lymphostasis, because of disrupted immune cell trafficking, creates a localized area of immunosuppression permitting latent human papillomavirus (HPV) in-

fection to manifest as warts.⁴ Macrophages ingest lipid-rich debris derived from overlying damaged and/or proliferating keratinocytes and accumulate in the papillary dermis because of poor lymphatic drainage. In corollary, increased lymphatic flow leads to regression of VX.² Based on this mechanistic framework, we sought to determine if histologic evidence of lymphedema existed in LS that would explain the relative frequent occurrence of VX in vulvar LS, 60% in the series reported by Fite et al.¹

Methods. Over a 3-month period in 2011, all diagnosed cases of LS in the Department of Pathology at Albany Medical College were retrieved. Formalin-fixed paraffin-embedded sections were immunostained with antibodies to D2-40, a lymphatic specific marker (Dako; 1:200) and CD68, a macrophage marker (Ventana Medical Systems; prediluted), using an automated method (Ventana Medical Systems). Normal skin from elliptical excisions of benign and malignant skin tumors was used for controls (cases previously reported⁴). Lymphatic density was measured by counting the number of D2-40 expressing vessels per millimeter squared. Lymphatic vessels were categorized as dilated or collapsed; the maximal dilation of the former was measured (methods previously described⁴). In addition, the presence or absence of D2-40 expression by the basal layer of the epidermis and aggregates of CD68-positive cells at the DEJ were recorded. STATA software, version 11.2 (StataCorp LP), was used for statistical analysis, with significance set at $P < .05$. The institutional review board of Albany Medical College approved this study.

Results. The **Table** lists the overall results of this study, revealing that LS specimens exhibited significantly more dilated lymphatics and greater dilation of lymphatic vessels than did controls. In addition, dilated lymphatics significantly outnumbered collapsed vessels in LS samples, whereas collapsed lymphatics significantly outnumbered dilated vessels in controls ($P \leq .03$). Notably, collapsed lymphatic vessels were seen underlying the sclerotic zone, often in areas of inflammation, but lymphangiectases were found throughout the zone of sclerosis, mostly in its deep aspect, which also contained dilated blood vessels. The D2-40 expression of basal keratinocytes was frequent in LS, a phenomenon that has been described in localized lymphedema.³ Conspicuously, CD68⁺ macrophages could be found forming small aggregates at the DEJ in more than half of LS cases (**Figure**).

Comment. Lichen sclerosus has been likened to an “inflammatory scar.” Therefore, it is not surprising to find that the hallmark feature of LS, its sclerosis, which progressively replaces the upper dermis over time, disrupts lymphatic drainage by effacing the normal dermal architecture, leading to signs of lymphostasis—numerous dilated lymphatic vessels. Scarring and lymphangiectases are ubiquitous features underlying warts and are suspected pathogenic factors.⁴

While only a few reports of VX have documented HPV infection,¹ the low frequency of detection has been attributed to the sensitivity and specificity of the methods used