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Osteopontin Expression in Spitz Nevi

Osteopontin (OPN)—a matricellular protein related to SPARC (secreted protein acid rich cysteine), thrombospondin, and tenascin C—is a secreted phosphoprotein that plays a crucial role in mediating cell-matrix interactions. The protein, first described in 1979 as a secreted phosphoprotein produced by malignant epithelial cell lines, has been shown to be overexpressed in numerous invasive carcinomas. It is postulated that OPN may facilitate invasion through extensive extracellular binding domains that include sites for hydroxyapatite, heparin, calcium, CD44v3, and numerous integrin heterodimers. In addition to the extracellular matrix–modulating properties, ligation of the OPN receptor on cells induces antiapoptotic effects. Other effects of OPN include induction of tissue matrix metalloproteinase 2, stress-dependent angiogenesis, and macrophage-directed interleukin-10 suppression.

Osteopontin expression in melanoma has been examined in several articles and shown to be elevated in most tumors. Because Spitz nevi and melanoma share certain histopathologic features, making diagnosis difficult at times, we examined the expression of OPN via immunohistochemical analysis in Spitz nevi, melanoma in situ, primary invasive melanoma, and metastatic melanoma. To determine whether OPN expression differs among these tumors.

Methods. This study was approved by the institutional review board of the University of Arkansas for Medical Sciences, Little Rock. Paraffin-embedded specimens of Spitz nevi, melanoma in situ, primary invasive melanoma, and metastatic melanoma were retrospectively retrieved by electronic query for a 3-month period of accessions. Twenty-one cases of Spitz nevi, 5 of melanoma in situ, 10 primary invasive melanomas, and 3 metastatic melanomas were identified. A 1:200 dilution of OPN monoclonal antibody (Laboratory Vision Co, Fremont, California) was used for standard techniques.

Slides were reviewed by 2 independent blinded observers (T.D.H. and H.L.W.). Tumor staining was graded on a 0 to 3 scale (0 indicating absence of staining; 1, sparse and weak staining; 2, moderate and diffuse staining; and 3, strong, intense, and diffuse staining). Mean±SD intensity of staining within each diagnostic group was calculated using R statistical analysis (R statistical analysis, version 2.2.0, www.r-project.org). Comparative staining intensity between the Spitz nevus group on the one hand and the primary invasive melanoma and metastatic melanoma groups on the other was analyzed using the Wilcoxon rank sum test.

Results. Spitz nevi demonstrated a mean±SD staining intensity of 0.76±0.74. Melanoma in situ averaged 0.8±0.4. Primary invasive melanoma and metastatic melanoma demonstrated a mean±SD score of 2.78±0.41 and 3.0±0, respectively. Cumulative scores are shown in the Figure. In concordance with Zhou et al, no correlation between depth of invasion and staining intensity was observed. One case of metastatic melanoma demonstrated a perinuclear dot pattern of staining. Overall, staining of Spitz nevi vs primary invasive melanoma and metastatic melanoma were significantly different (P<.001).

Comment. Spitz nevi are commonly encountered melanocytic neoplasms that may histologically resemble melanoma. Spitz nevi may display features such as pagetoid growth, desmoplasia, pleomorphism, and dermal mitoses, which may make differentiation difficult.

Various markers have been studied to differentiate Spitz nevi from melanoma. Kapur et al have demonstrated a difference in the expression of fatty acid synthetase, p21, and Ki-67 in Spitz nevi vs melanomas. The study found a statistically significant difference in fatty acid synthase expression in “typical” vs “atypical” Spitz nevi and suggested that atypical Spitz nevi represent a distinct intermediate entity between typical Spitz nevi and melanoma. Recently, comparative genomic hybridization (CGH) techniques are being applied in spitzoid melanocytic tumors with promising results. Bastian et al have shown through CGH that a minority of Spitz nevi demonstrate amplification of the p arm of chromosome 11, which is associated with alterations in HRAS expression. Importantly, no melanomas examined demonstrated similar 1p amplifications, but rather, all had an array of other chromosomal aberrations not seen in Spitz nevi.

Figure. Scatterplot demonstrating the numbers of cases at each staining score and the mean±SD staining score in each type of melanocytic tumor examined.

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In conclusion, we report the staining characteristics of OPN in Spitz nevi and confirm the previously reported findings of OPN in primary invasive, metastatic, and in-situ melanomas. Spitz nevi do not express significant levels of OPN compared with primary invasive melanoma and metastatic melanoma. This difference was statistically significant. The limitations of the present study include the relatively small number of cases examined and the subjectivity that is inherent in immunohistochemical analysis. Validation of OPN’s role in Spitz nevi will require substantially larger study sizes and possibly the use of morphometric analysis methods to improve objectivity in assessing OPN expression strength. The diagnostic utility of differential OPN expression is likely to be small in the practice of dermatopathology. Including OPN expression in CGH analysis may heighten the sensitivity and specificity of this technique.

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COMMENTS AND OPINIONS

Long-term Follow-up of a Child Treated With Efalizumab for Atopic Dermatitis

I appreciate the observations and comments made by Rapaport in the February issue of the Archives and agree that a subset of patients with chronic eczema experience corticosteroid dependence and rebound flare. This is probably more common in adults, especially among those who have been treated with long-term topical corticosteroids on the face and groin. Another subset of patients with eczema have severe atopic dermatitis that does not reliably respond to any of the “panoply” of other described options.

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Figure 1. In September 2005, excellent clearing of eczema is evident after 3 months of efalizumab treatment.