Melanocytic Nevi with Spitz Differentiation: Diagnosis and Management

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ABSTRACT

Spitz lesions comprise a diverse group on the histologic continuum ranging from a papule or nodule that is usually less than 1 cm. In a small number of cases, they can be moderately or markedly pigmented. The cheeks and ears are the favored sites in children, and in adults, the limbs and trunk are most commonly involved.

Even though the majority of melanocytic proliferations with Spitzoid differentiation can be classified as benign Spitz nevi or Spitzoid melanomas based on histopathologic and clinical criteria (Table 1), there is a subset in the central portion of the continuum that challenge even the most experienced dermatopathologist. Terms to describe this category include dysplastic Spitz nevus, atypical Spitz tumor, or Spitz tumor of uncertain malignant potential. Although these problematic neoplasms display architectural and cytologic atypia to a degree beyond benign Spitz nevus, the atypia is not sufficient for a diagnosis of Spitzoid melanoma. Due to the challenge in distinguishing atypical Spitz nevus from Spitzoid melanoma using light microscopy, other diagnostic techniques have been investigated including immunohistochemistry and dermatfiber analysis.

The advent of CGH has played a pivotal role in the diagnosis of Spitz lesions. CGH is a molecular-cytogenetic method that analyzes copy number changes in the DNA content of Spitz lesions. It is capable of detecting loss, gain, and amplification of the DNA copy number at the chromosomal level. Based on CGH analysis, Spitzoid melanomas have higher overall number of chromosomal abnormalities compared to benign Spitz nevi. On the other hand, CGH analysis showed no or minimal copy number increase in chromosomal 1p in a subset of Spitz lesions. This copy number increase is associated with mutations of HRAS. HRAS is a small GTPase and a member of the RAS family of genes, which are protooncogenes involved in cellular signal transduction. HRAS activation could explain some of the histologic features that overlap with Spitzoid melanomas. Copy number increase of chromosome 1p and the associated HRAS mutation do not occur in Spitzoid melanomas. Therefore, chromosomal gains of 1p and the absence of chromosomal aberrations in most Spitz nevi may be in the distinction of certain lesions. These atypical features may make histopathologic distinction from Spitzoid melanoma difficult.

Although these diagnostic tools are promising, currently there is no technique that unequivocally identifies the borderline Spitz lesions and Spitzoid melanomas. In these situations, we believe that sentinel node biopsy plays an important role in making the final decision regarding management. According to Amin and Ackerman, the presence of atypical cells within the sentinel node prove malignancy. Therefore, melanocytic nevi with atypical cells within the sentinel node should be reclassified and managed as Spitzoid melanoma.

Recommendations for the management of melanocytic nevi with Spitz differentiation reported in the literature include observation, subtotal excision, or complete excision. However, we believe that all lesions with Spitz differentiation must be excised completely. Since Spitzoid melanoma can arise within benign Spitz nevi, we recommend wide local excision with 5 mm margins of benign Spitz nevus. Sentinel lymph node biopsy is not recommended in these cases. On the other hand, we believe that the staging and management of Spitzoid melanoma should follow the National Comprehensive Cancer Network (NCCN) guidelines.

Although the management of atypical Spitz nevi is controversial, we agree with Luddgate et al. that these lesions require 1 cm margins. SLNB should be performed in lesions that are >1 cm in diameter. In lesions that are 2-5 cm, the use of sentinel node biopsy is considered. The presence of atypical cells within the sentinel lymph node confirms the diagnosis of Spitzoid melanoma, and the management should follow the NCCN management guidelines for melanoma.

CONCLUSIONS

In this article, we have attempted to portray the current state of the art involving melanocytic proliferations with Spitz differentiation. Distinguishing among the three categories can be challenging. Melanosis and differentiation, in these cases have been reported and can have devastating consequences. The management of these patients should not be undertaken until it is confirmed potentially with corroborative immunohistochemical analysis. The presence of atypical cells within the sentinel lymph node confirms the diagnosis of Spitzoid melanoma, and the management should follow the NCCN management guidelines for melanoma.

REFERENCES