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Imaging mass spectrometry- A novel ancillary method for the diagnosis of malignant melanoma

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Abstract

Spitzoid neoplasms are melanocytic lesions that include a spectrum ranging from completely benign ‘‘classic’’ Spitz nevi to malignant melanomas that show ‘‘Spitzoid’’ features. The gold standard for diagnosing Spitz nevus (SN) and differentiating it from Spitzoid malignant melanoma (SMM) is histopathologic examination applying well established criteria. However, there are melanocytic lesions that show conflicting histopathologic criteria and the distinction between a benign SN and SMM may be extremely difficult. We performed Imaging Mass Spectrometry analysis on formalin-fixed, paraffin embedded (FFPE) tissue samples to identify differences on proteomic level between SN and SMM. The diagnosis of SN and SMM was based on histopathologic criteria, clinical features, and follow-up data. The melanocytic component from 114 cases of SN and SMM from the Yale Spitzoid Neoplasm Repository were analyzed. After obtaining mass spectra from each sample, classification models were built using a training set of biopsies from 26 SN and 25 SMM. The classification algorithms developed on the training data set were validated on another set of 30 samples from SN and 33 from SMM. We found proteomic differences between the melanocytic components of SN and SMM and identified 5 peptides that were differentially expressed in the 2 groups. From these data, 29 of 30 SN and 26 of 29 SMM were recognized correctly in the validation set. This method correctly classified SN with 97% sensitivity and 90% specificity in the validation cohort. Imaging Mass Spectrometry analysis can reliably differentiate benign nevi from malignant melanomas in FFPE tissue based on proteomic differences.

Biography

Rossitza Lazova, MD has completed a residency in Anatomic and Clinical Pathology and a fellowship in Dermatopathology with Dr. A. Bernard Ackerman. She is an Associate Professor of Dermatology and Pathology and Director of the Dermatopathology Fellowship at Yale University. Dr. Lazova has published more than 60 papers in reputed journals and is an author of a textbook titled Atlas of Practical Mohs Histopathology. She has established the Yale Spitzoid Neoplasm Repository and is an internationally recognized expert in the field of Spitzoid melanocytic neoplasms. She has pioneered the use of Mass Spectrometry in the diagnosis of difficult melanocytic lesions.