In vivo reflectance confocal microscopy is a novel technique for the noninvasive study and diagnosis of the skin. The aim of this study was to describe and characterize the cytological and architectural aspects of cell clusters in melanocytic lesions observed by confocal microscopy, and to correlate them with routine histopathology. A total of 55 melanocytic lesions comprising 20 melanomas, 25 acquired nevi and 10 Spitz nevi were studied by means of reflectance confocal microscopy, dermoscopy and routine histopathology. Three different types of cell clusters at confocal microscopy observation (dense, sparse cell and cerebriform clusters) were identified and correlated with histopathology. Dense clusters appeared characteristic for benign lesions, although present in 13 out of 20 melanomas. Sparse cell clusters were more frequently observable in melanomas, but also sporadically present in one Spitz nevus. Moreover, cerebriform clusters were exclusively observed in five out of 20 melanomas. Confocal microscopy allowed the in vivo characterization of aspects of melanocytic nests and their exact correlation with histopathology.