**ABSTRACT**

**OBJECTIVES:** To characterize nodular melanoma (NM) using dermoscopy, in vivo reflectance-mode confocal microscopy, and histopathologic analysis.

**DESIGN:** Consecutive pure NMs and superficial spreading melanomas (SSMs) with nodular or blue areas were studied using dermoscopy and confocal microscopy, and a correlation with histopathologic findings was performed.

**MATERIALS:** Ten NMs, 10 SSMs with a nodular area, and 10 SSMs with a blue palpable but not yet nodular area.

**MAIN OUTCOME MEASURE:** Confocal differences within the nodular component between pure NMs and SSMs with a nodular area, hypothesizing different biological behaviors.

**RESULTS:** Whereas NMs had predominantly nonspecific global dermoscopic patterns, SSMs exhibited a multicomponent pattern and higher dermoscopic scores. Globules, blue-white veil, atypical vessels, and structureless areas were frequent in NMs and in nodular areas from SSMs. At confocal microscopy, NMs exhibited few pagetoid cells within a typical epidermal architecture in the superficial layers in most cases, differing from SSMs frequently characterized by epidermal disarrangement and pagetoid infiltration. At the dermoepidermal junction, dermal papillae were rarely seen in nodular areas both from NMs and from SSMs, frequently substituted by nonaggregated atypical cells distributed in sheet like structures. In the upper dermis, all groups exhibited plump bright cells, dense dishomogeneous cell clusters, and atypical nucleated cells, whereas cerebriform clusters were characteristic of NMs. Conclusion Distinctive dermoscopic and confocal features seen in NMs compared with SSMs are helpful in making the diagnosis and suggest different biological behavior.