

Inner gray halo, a novel dermoscopic feature for the diagnosis of pigmented actinic keratosis: Clues for the differential diagnosis with lentigo maligna

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Background: Pigmented actinic keratosis (PAK) is a frequent simulator of lentigo maligna (LM) on the face upon clinical and dermoscopic examination, leading to misdiagnosis and unnecessary excisions. LM and PAK share dermoscopic features, making it difficult to have a confident diagnosis of PAK only with current dermoscopic knowledge.

Objective: We sought to evaluate sensitivity, specificity, and interobserver reproducibility of a novel dermoscopic feature, inner gray halo (IGH), and establish its histopathological and confocal correlations.

Methods: Dermoscopists blinded to histopathological diagnosis evaluated 58 PAK and 21 LM for the presence of IGH and dermoscopy parameters. Areas exhibiting IGH were marked and imaged with reflectance confocal microscopy before sampling for histopathologic correlation. Reflectance confocal microscopy and transverse histologic sectioning were performed in 14 of 79 cases.

Results: IGH was present in 53 of 58 (94.1%) PAK and in 5 of 21 (23.8%) LM in our series (sensitivity 91.4%; specificity 71.4%; positive predictive value 89.8%). Interobserver agreement was excellent (Kappa 0.846). Through transverse and perpendicular histologic sections, a dermoscopic-histologic-confocal correlation of IGH was established.

Limitations: A larger test set is needed to further validate the use of IGH in the differential diagnosis of PAK and facial pigmented lesions.

Conclusion: IGH is a novel dermoscopic parameter useful for the differentiation of PAK from LM on the face. (J Am Acad Dermatol <http://dx.doi.org/10.1016/j.jaad.2014.05.025>.)

Key words: confocal; dermoscopy; face; histopathology; lentigo maligna; pigmented actinic keratosis.

Pigmented actinic keratosis (PAK) of the face represents a challenging lesion on clinical and dermoscopic examination, which is frequently misdiagnosed as lentigo maligna (LM).¹⁻⁴ Whereas LM should be excised, PAK can be treated with less invasive approaches and excellent aesthetic results.^{5,6} However, diagnosis is frequently obtained after biopsy, leading to unnecessary scars on a cosmetically sensitive area. Up until now, the

Abbreviations used:

CI:	confidence interval
IGH:	inner gray halo
LM:	lentigo maligna
PAK:	pigmented actinic keratosis
RCM:	reflectance confocal microscopy

dermoscopic features described for differential diagnosis of LM with other pigmented freckles of

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the face include several parameters, such as asymmetric pigmented follicular openings, dark (brown or black) rhomboidal structures, slate-gray globules and slate-gray dots, hyperpigmented rim of follicular openings, slate-gray streaks and dark streaks, annular-granular pattern, and black blotches.⁷⁻⁹ These features are frequently found on PAK. Only black blotches¹ were specific for LM, but this represents a late parameter rarely present in early lesions.⁹ On the other hand, dermoscopic features described for actinic keratosis, such as neighborhood sign, strawberry sign, and hair follicle openings filled with yellowish keratotic plug and surrounded by a white halo in a targetoid appearance, apply mostly for light PAK,^{2,3} whereas deeply pigmented lesions remain difficult to differentiate from LM.

In our experience, the presence of inner gray halo (IGH), a subtle homogeneous gray or beige halo that surrounds follicular openings (or follicular plugs), forming a sort of “internal ring” to the brown meshes of the pseudonetwork,¹⁰ is frequently seen in PAK.

In this article we sought to explore clinical usefulness of this new feature and to identify its histologic correlate through *in vivo* confocal microscopy and histologic transverse sectioning.¹¹

METHODS

This study was approved by the ethics committees of Federal University of São Paulo—Escola Paulista de Medicina (UNIFESP-EPM) and of A. C. Camargo Cancer Center, São Paulo, Brazil.

Study population

All lesions excised at the Pigmented Lesions Unit—Dermoscopy Group of the Federal University of São Paulo—Escola Paulista de Medicina (UNIFESP-EPM) during the period of 2003 through 2012, with a histopathologically confirmed diagnosis of LM or PAK and available dermoscopic images, were considered for the study.

Moreover, a series of PAK and LM between 2012 and 2013 were also documented by means of reflectance confocal microscopy (RCM) (A. C. Camargo Cancer Center) before excision and histopathology procedure for transverse sectioning was applied for exact correlate identification.¹¹

Instruments

Dermoscopic images were acquired using $\times 10$ magnification with Dermaphot (Heine Optotechnik, Herrsching, Germany) and a Nikon FM1 reflex camera (Nikon Corp, Tochigi, Japan) or Delta 20 (Heine Optotechnik) mounted on a Nikon Coolpix 4300 digital camera or Nikon J1 digital camera (Nikon Corp).

RCM images were acquired using the near-infrared reflectance confocal laser microscope (Vivascope 1500, Caliber I.D., Rochester, NY). The technique and the acquisition procedure are presented elsewhere. For this specific study, horizontal tissue images, ranging from 4×4 - to 8×8 -mm sections, depending on the size of the analyzed lesion, producing a mosaic image (Vivablock), were acquired for all lesions. The global pattern on dermoscopy was correlated with the

mosaic image at the level of the granular layer, spinous layer, and dermoepidermal junction of the epidermis. Sequentially deeper individual images centering the hair follicle were acquired from the corneal layer to the papillary dermis (Z-axis stack, $1.5\text{-}\mu\text{m}$ steps up to $150\ \mu\text{m}$)¹² and were used for RCM correlation of the IGH parameter.

Routine histopathology and transverse sections

Hematoxylin-eosin slides from all cases were obtained. In selected cases, transverse sections of IGH area were performed to obtain exact correlation with RCM images. Guided by dermoscopy, the site of the IGH was marked with a 4-mm punch during surgery. The punch biopsy specimen was processed for vertical and transverse sections as previously described.¹¹ Fontana-Masson stain and immunohistochemical reactions, including antibodies for cytokeratins A1 and A3, and human melanoma black monoclonal antibody (HMB-45) were performed as necessary for routine dermopathological evaluation.

Parameter evaluation

Dermoscopy. Two dermatologists highly experienced in dermoscopy (S. Y. and G. R.), blinded to histopathological diagnoses, received a brief training on the new feature IGH and were asked to evaluate all the study lesions for the presence or absence of IGH. The observers were also asked to

CAPSULE SUMMARY

- Pigmented actinic keratosis is a common simulator of lentigo maligna, as the 2 lesions share several clinical and dermoscopic features.
- Inner gray halo is a novel dermoscopic feature of pigmented actinic keratosis, with strong histologic and reflectance confocal microscopy correlates.
- Inner gray halo may assist in the differentiation of pigmented actinic keratosis from lentigo maligna.

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