Diagnosis of congenital pigmented macules in infants with reflectance confocal microscopy and machine learning

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To the Editor

Congenital pigmented macules (CPM) can be clinically and dermoscopically equivocal in infants, making the differential diagnosis between Café au Lait Spot (CLS) and Congenital Melanocytic Nevus (CMN) difficult. Reflectance confocal microscopy (RCM) may reveal morphological patterns, differentiating CMN from CLS at the bedside and changing management/follow-up of these lesions.

A retrospective study was performed to describe the RCM patterns of dermoscopically equivocal CPM and to compare it on CLS and CMN. CPM cases were analysed and classified either CLS or CMN by a skin biopsy or by clinical characteristics and/or dermoscopical evolution during follow-up. RCM acquisition took 5-30 minutes per patient (handheld RCM Vivascope 3000® -CALIBER, Rochester, NY, USA). Frequencies of each clinical and RCM pattern for CLS and CMN were calculated.[1] Images evaluation was performed by three experts in a blinded manner and the inter-expert agreement was analysed. Finally, a pretrained convolutional neuronal network combined with a Support Vector Machine algorithm, was trained to automatically classify CLS and CMN based on RCM images at the dermal-epidermal junction.

Among 30 children with CPM (mean age 33.7 months; standard deviation (SD) 31 months), 20 patients were diagnosed with CLS and 10 with CMN. The mean follow-up duration was 72 months (SD 40). CPM locations were: face (33%), back (23%), abdomen (20%), arms (3%) and legs (20%). Clinically, hair was more commonly observed on CMN than CLS, however no significant difference was observed for lesion's color or regular/irregular border. 7943 RCM images from 30 patients, were acquired at first dermatology consultation. RCM images of CMN (figure 1) were the only class characterized by the presence of nests (CMN: 100% *vs* CLS:0%, p <0,001). In contrast, RCM images of CLS (figure 2) were characterized by the presence of bright peri-papillary rings (CLS: 100% *vs* CMN: 30%,

p <0.001) and enlarged peri-papillary rings (CLS: 100% *vs* CMN: 10% p <0.001). Honeycomb and cobblestone epidermis patterns usually described on RCM images and presence of melanophages on the dermis were studied and not significantly different between both sets. The blind retrospective evaluation exhibited an excellent inter-observer agreement for the presence of nests and bright peri-papillary rings (kappa coefficient (κ) = 1) and enlarged peri-papillary rings (κ = 0.84). The classifier by cross-validation showed an accuracy of 89.1% to discriminate CMN to CLS with respectively 85.5% and 92.8% of good predictions.

There are very few data describing CMN and CLS diagnostic criteria in RCM in infants. Prodinger *et al.*[2] demonstrated the diagnostic value of RCM in a single case of nevus spilus. Zeng *et al.*[3] described the RCM characteristics of facial hyperpigmented lesions in a series of adults.

Our results demonstrated that CLS can be differentiated from CMN by specific characteristics and different patterns on RCM images. Machine learning can be combined with RCM to assist the image's interpretation and to increase the diagnostic accuracy in the differentiation of CPM. RCM seems to be a non-invasive helpful diagnostic tool in difficult to diagnose and dermoscopically equivocal CPM cases.

References

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Figure 1:

RCM at the level of the dermal epidermal junction showing numerous bright melanocytic nests: congenital melanocytic nevus

Figure 2:

RCM at the level of the dermal epidermal junction showing bright and enlarged peripapillary rings: café-au-lait spot.