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Melanoma and satellite blue papule

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ABSTRACT The colors that are seen in dermoscopy depend on the anatomic level of the skin at which the chromophores are seen. Blue color can be found in a variety of melanocytic and nonmelanocytic lesions.

An 89-year-old man presented with a 3-year history of a slow-growing, hyperpigmented patch located on the distal third of the right arm. Dermoscopy showed an atypical network, irregularly distributed globules, pigmented internal streaks and a milky-red area. Based on these findings a diagnosis of slow-growing malignant melanoma was made. Simultaneously, a well-defined blue papule was seen on the proximal third of the same arm. Dermoscopy disclosed a homogeneous blue pattern. After clinical and dermoscopic correlation our differential diagnosis for this blue lesion included cutaneous melanoma metastasis, blue nevus and foreign body reaction. The patient recalled its onset 75 years ago after a grenade explosion. We also discuss the blue lesion appearance under reflectance confocal microscopy and high-definition optical coherence tomography. Histopathological examination after excision of the hyperpigmented patch and blue papule revealed a melanoma in situ and a foreign body reaction, respectively.

The diagnostic evaluation of a blue lesion should always rely on the integration of all data, especially clinical and dermoscopic features. Other non-invasive techniques, like reflectance confocal microscopy and high-definition optical coherence tomography can also be important aids for its differential diagnosis.

Case presentation

An 89-year-old Caucasian man presented to our clinic with a 3-year history of an asymptomatic, slow-growing, hyperpigmented skin lesion located on the distal third of the dorsal aspect of the right arm. The patient had no personal or family history of skin cancer. The physical examination revealed an asymmetrical, ill-defined brown patch with 21 mm of maximum diameter (Figure 1). Dermoscopy examination of the lesion disclosed an atypical network, irregularly distributed brown and black globules, pigmented internal

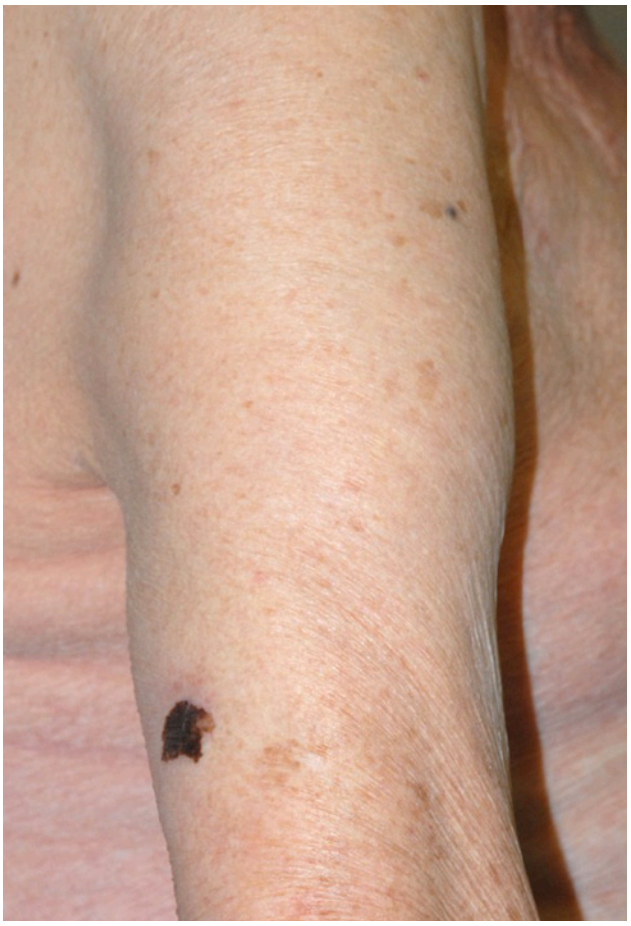

Figure 1. Simultaneously observed irregular brown patch (distal third) and blue papule (proximal third) on the dorsal aspect of the right arm. [Copyright: ©2014 Oliveira et al.]

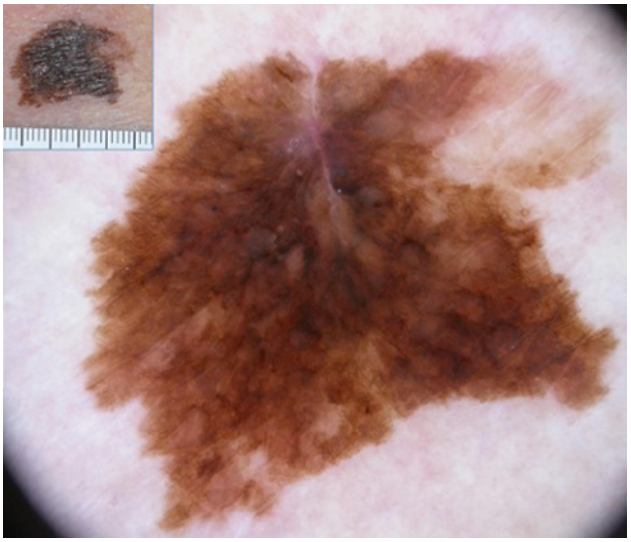

Figure 2. Dermoscopy observation (brown patch): atypical network, irregular brown and black globules, pigmented internal streaks and milky-red area. [Copyright: ©2014 Oliveira et al.]

streaks and a milky-red area (Figure 2). Based on clinical and dermoscopic findings a diagnosis of slow-growing malignant melanoma was made. Lymph node inspection was unremarkable. Simultaneously, a well-defined blue papule with 4 mm

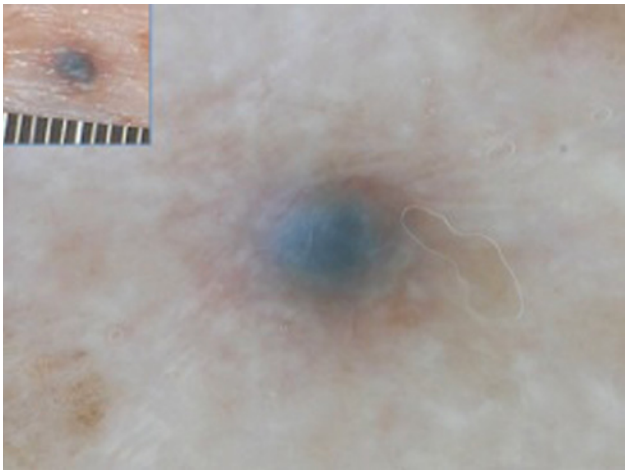

Figure 3. Dermoscopy observation (blue papule): homogeneous blue pattern. [Copyright: ©2014 Oliveira et al.]

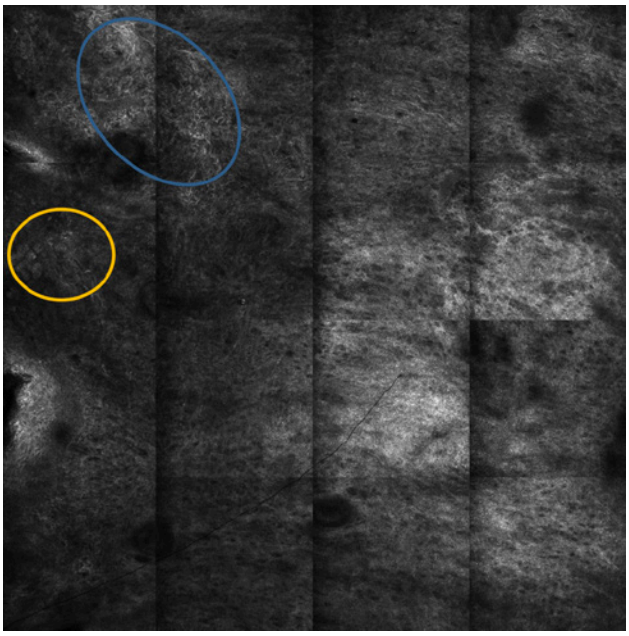

Figure 4. Reflectance confocal microscopy examination (mosaic 2 x 2 mm): normal honeycomb pattern, edged-papillae, absence of atypical cells and dendritic melanocytes in the dermis; elongated cords and bulbous projections (yellow circle), flattened junction and moderately refractive lace-like material adjacent to collagen bundles (blue circle) were also seen at the upper dermis. [Copyright: ©2014 Oliveira et al.]

of maximum diameter was seen on the proximal third of the dorsal aspect of the same arm (Figure 1). Dermoscopy showed a homogeneous blue pattern (Figure 3). The diagnosis of cutaneous melanoma metastasis was immediately suspected. The patient was then asked for its onset and evolution. He remembered this blue lesion for 75 years. The diagnosis of common blue nevus was also considered. The patient added that the papule followed local skin injuries from a grenade explosion during the II World War. Therefore, foreign body reaction and traumatic pigmentation were also included in the differential diagnosis.

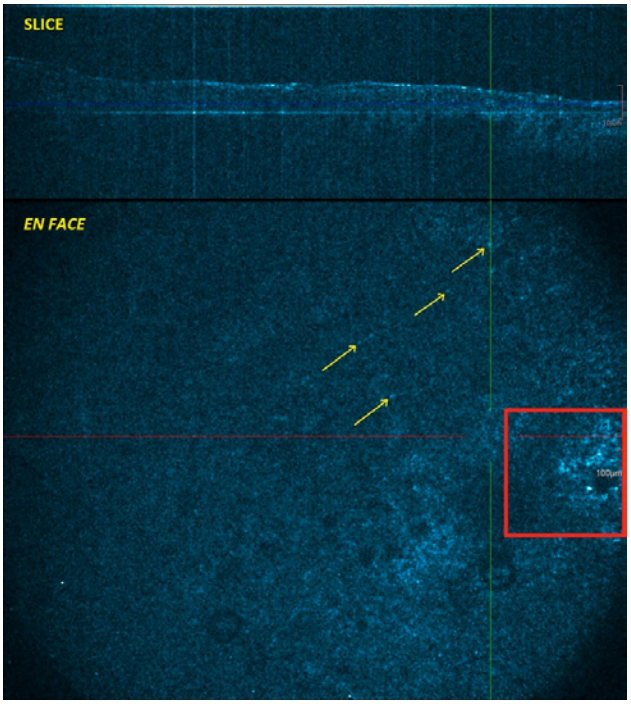

Figure 5. High-definition optical coherence tomography (slice and en face mode): scattered highly refractile inflammatory cells (yellow arrows) and aggregates of brightly refractile particles (red square) in the deeper dermis. [Copyright: ©2014 Oliveira et al.]

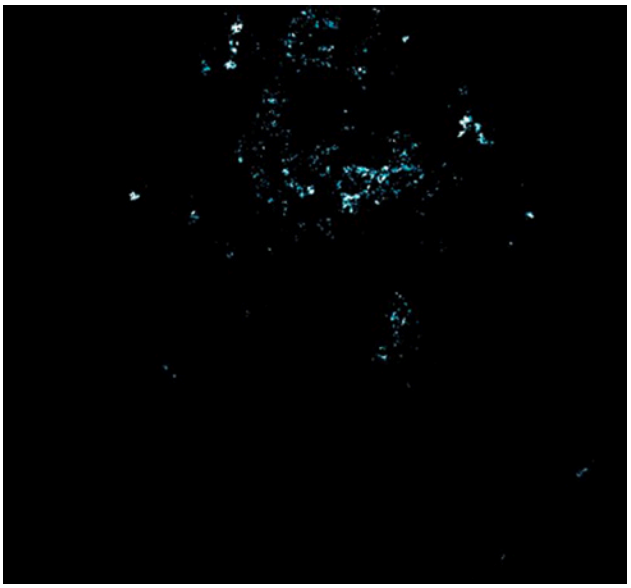

Figure 6. High-definition optical coherence tomography features of aggregates of highly refractile particles in the deeper dermis were better represented under histogram "image splitter," possibly corresponding to foreign body. [Copyright: ©2014 Oliveira et al.]

The blue papule was further examined by reflectance confocal microscopy (RCM) and high-definition optical coherence tomography (HD-OCT). RCM (VivaScope1500®; Lucid Inc., Rochester, N.Y., USA) evaluation was unremarkable, with normal honeycomb pattern, edged-papillae in the dermal-epidermal junction, and absence of atypical cells and dendritic melanocytes in the superficial dermis. Some changes attributed to chronic sun exposure were seen, including elongated cords, flattened junction and moderately refractive lace-like material adjacent to collagen bundles, correlating to solar elastosis at the upper dermis (Figure 4). HD-OCT (Skintell®, AgfaHealthCare, Belgium) en face mode enabled the observation of scattered bright inflammatory cells in the dermis and clusters of bright coarse particles in the deeper dermis (Figure 5). These particles were better represented using OCT histogram "image splitter" in which the number of pixels with specific values is isolated in an image (Figure 6).

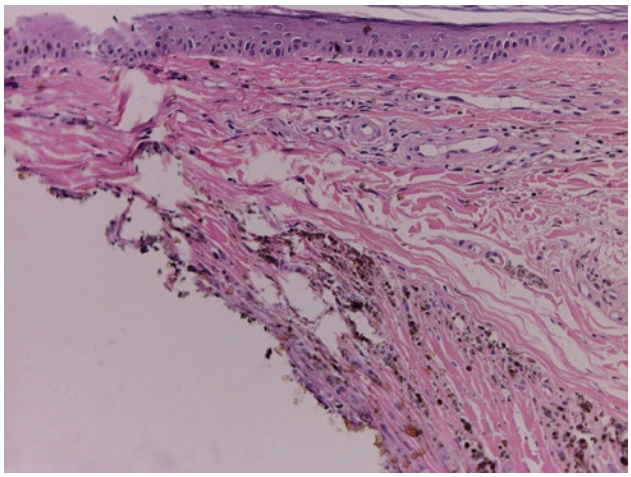

Figure 7. Histopathological examination of the blue papule showed a foreign body with fibrosis and sparse inflammatory infiltrate (hematoxylin-eosin, x100). [Copyright: ©2014 Oliveira et al.]

Both lesions were excised. Subsequent histopathological examination of the hyperpigmented patch confirmed the diagnosis of melanoma in situ, while the examination of the blue papule revealed a foreign body with fibrosis and sparse inflammatory infiltrate (Figure 7).

Conclusions

Several non-invasive imaging techniques have emerged in recent years aiming for higher accuracy of in vivo diagnosis. These include dermoscopy, reflectance confocal microscopy (RCM) and high-definition optical coherence tomography (HD-OCT).

The colors that are seen in dermoscopy depend on the anatomic level of the skin at which the chromophores (melanin, hemoglobin, collagen) are seen. Blue color can be found in a variety of melanocytic and nonmelanocytic lesions. Its diagnosis can be challenging especially if a diffuse bluish pigmentation is found under dermoscopy. The differential diagnosis of melanocytic lesions with blue color should include blue nevus, Spitz nevus, malignant melanoma and cutaneous melanoma metastasis. Blue hue can also be seen in nonmelanocytic lesions like seborrheic keratosis, including lichen planus-like keratosis, hemangioma, pigmented basal cell carcinoma, hemosiderotic dermatofibroma, Kaposi sarcoma and

angiosarcoma. Finally, exogenous dermal blue pigmentation, such as ink tattoo, radiation tattoo, and traumatic penetration of foreign pigmented materials.

Our differential diagnosis for this blue lesion included CMM, common blue nevus and foreign body reaction/exogenous pigmentation.

Cutaneous melanoma metastasis was our first and immediate diagnosis because of the simultaneous observation of a suspected melanoma and a blue lesion with homogeneous blue color under dermoscopy, and located in proximity to the primary melanoma. However, the suspected melanoma lesion had a slow-growing progression, and dermoscopy revealed asymmetrical network, irregular globules and internal streaks, which were a clue for a thin melanoma. The diagnosis of CMM is usually suspected based on a history of primary invasive, thick melanomas [2]. The lesion history with a 75-year duration of onset also allowed for the clinical exclusion of CMM. The clinical and dermoscopic diagnosis of common blue nevus was then considered relying on the dermoscopic observation of diffuse, homogeneous bluish pigmentation, in absence of specific melanoma criteria, on a long-standing, stable lesion [3]. The possible post-traumatic relation to the onset of the lesion made us include the diagnosis of exogenous traumatic pigmentation, usually also associated with a blue structureless pattern in dermoscopy.

Since dermoscopy was not conclusive RCM examination of the blue papule was performed. RCM allows for the visualization of microscopic features in vivo with a nearly histological resolution. Increasing knowledge on the RCM appearance of a wide range of skin lesions may help us to improve our bedside diagnostic accuracy [4]. The findings of normal honeycomb pattern and lack of atypical cells and dendritic melanocytes in the superficial dermis allowed the exclusion of CMM and blue nevus in the examined skin levels. However, limited laser depth penetration (250 μm) hampers visualization of the deep dermis representing a limitation of RCM in the assessment of both CMM and common blue nevus [5,6].

HD-OCT is a recently introduced technique based on the same principles of conventional OCT but differing on its ability to give optical imaging up to 570 μm deep within the skin with high resolution of 3 μm both in axial and lateral directions. This technique is capable of capturing not only slice but also en face images in real time and fast three-dimensional acquisition. Therefore, HD-OCT allows in vivo examination of the skin enabling visualization of individual cells with a greater depth than RCM. En face mode imaging and histogram representation showed scattered highly refractile inflammatory cells and aggregates of brightly refractile particles in the deeper dermis [7,8]. It was also possible to exclude CMM and blue nevus, in a greater depth penetration using HD-OCT. En face and histogram changes possibly corresponded to foreign body material and inflammation associated to the skin trauma reported by the patient that took place 75 years ago.

The definite diagnosis in our case was made with the histopathological examination that revealed a foreign body in the deeper dermis, a possible consequence of the grenade explosion, showing good correlation with the HD-OCT findings of large bright refractile particles in the same location.

The deeper location of foreign material in our case caused a bluish appearance, both in clinical and dermoscopic presentation. It can be explained by a similar phenomenon as seen with dermal melanin: the Tyndall effect of the physical light scattering effect of blue pigmentation in the dermis.

In conclusion, the diagnostic evaluation of a blue lesion should always rely on the integration of all data, including patient's age, duration of onset and rate of growth of the lesion, palpability and dermoscopic features [1]. Other non-invasive techniques, like RCM and HD-OCT can also be important aids in the differential diagnosis of a blue lesion. HD-OCT showed good correlation to the histopathological features of foreign body reaction.

As a rule all blue lesions that not fulfil clinical and dermoscopic criteria for a specific benign lesion should be excised. That was particularly true in our case due to the puzzling simultaneous clinical appearance of a melanoma and blue lesion. Even with a very long history of "blue."

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