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Non-choroidal yellow melanoma showing positive staining with Sudan Black consistent with the presence of lipofuscin: a case report

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ABSTRACT A case of a predominantly yellow primary superficial spreading melanoma arising on the back of a 44-year-old woman is presented. Possible causes of the clinical and dermatoscopic yellow color are discussed. Staining with the histochemical stain, Sudan Black, revealed a differential uptake compared to a closely matched control melanoma. We speculate that the clinical and dermatoscopic yellow color could be due to the presence of increased amounts of the pigment lipofuscin, which is known to produce subtle orange color in some choroidal melanomas.

Case report

A 44-year-old female patient presented to a dermatologist in Blanquefort, France for a routine check of her moles. There was no family or personal history of cutaneous malignancy and there was no history of any significant health problems or of any symptoms of disease. There had been a previous examination by the same dermatologist one year earlier, and nothing of concern had been noticed.

Examination revealed that the patient had skin of Fitzpatrick photo-type 3, with multiple ephelides as evidence of previous sun exposure. On the skin over her right scapula a raised, smooth, shiny, yellow and skin-colored lesion was observed (Figure 1). A dermatoscopic examination was performed (Figure 2), and the lesion was noted to be structureless, predominantly yellow. There was evidence of light melanin pigmentation with some areas of structureless gray interspersed between the dominant yellow areas and present

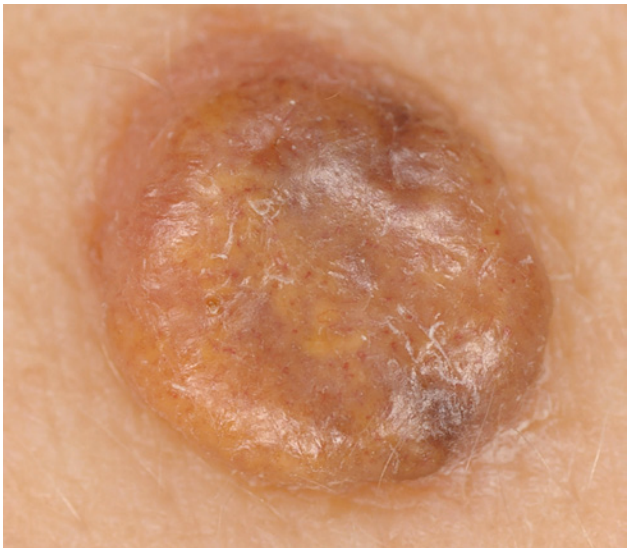

Figure 1. Close-up image (Pentax DS camera, Pentax Ricoh, Tokyo, Japan) of a nodular lesion over the right scapular area of a 44-year-old female patient. Irregular dominant yellow color is apparent. [Copyright: ©2014 Jegou Penouil et al.]

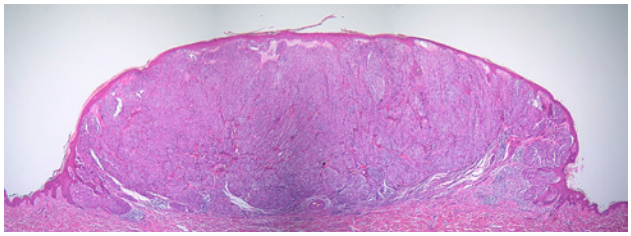

Figure 3. Dermatopathologic overview of the lesion shown in Figures 1 and 2. Significant nodular morphology is apparent although close examination of additional dermatopathology sections revealed that strict criteria for the classification as nodular subtype were not met. [Copyright: ©2014 Jegou Penouil et al.]

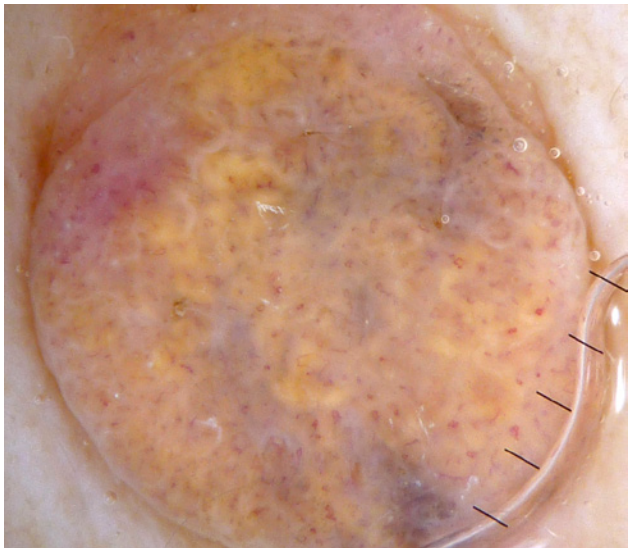

Figure 2. Dermatoscopy image (Heine delta 20 dermatoscope [Heine, Optotechnic, GmbH, Hersching, Germany] manually coupled to a Panasonic Lumix DMC ZX1 camera [Panasonic Corp., Kadoma, Japan]) of the lesion shown in Figure 1. The pattern is structureless, predominantly yellow, with an eccentric structureless pink area (upper pole of image) and evidence of light melanin pigmentation with some areas of structureless gray interspersed between the dominant yellow areas but absent at the upper pole of the image with resulting asymmetry. Polymorphous linear vessels (serpentine, looped and curved) are arranged randomly and densely over the surface of the lesion. There are a small number of dot vessels. [Copyright: ©2014 Jegou Penouil et al.]

at one end of the lesion but not the other producing asymmetry of color. Polymorphous linear vessels (serpentine, looped and curved) were arranged randomly and densely over the surface of the lesion and there were a small number of dot vessels.

Immediate excision biopsy was performed. Dermatopathologically (Figures 3-7) the lesion presented as a nodular, well circumscribed proliferation of melanocytes (Figure 3). There was a proliferation of cytologically abnormal melanocytes and some confluent nests of melanocytes at the dermoepidermal junction (Figure 5), and the junctional proliferation did extend beyond the dermal proliferation for more than three rete ridges at one location at the periphery of the nodular component. In the dermis sheets of abnormal melanocytes, most as spindle cells (Figures 5, 6A & B) and others with plump oval nuclei, prominent nucleoli and abundant clear cytoplasm (Figure 6A, B, C, D), extended throughout the dermis with both nesting and evidence of melanin production all the way to the base of the lesion (Figures 4 and 6). Melanin was seen on hemotoxylin and eosin staining (Figure 6A), which was also verified by Masson Fontana stain that confirmed significant melanin extending to the base of the melanocytic proliferation. Evidence of a pre-existing nevus was present as a sheet of mature nevomelanocytes at the base of the lesion (Figure 6D). The diagnosis was rendered melanoma, superficial spreading subtype with a dominant nodule comprising the great majority of the lesion, Breslow thickness 2.4 mm with 4 mitoses per high power field.

Following this, in an attempt to clarify the cause of yellow color, two further stains were performed.

A pearl's stain confirmed the absence of hemosiderin.

To test for the presence of the pigment lipofuscin, new sections were cut from the paraffin block, five microns in thickness and stained with Sudan Black. When this appeared to stain heavily, new sections of the same thickness were also cut from the paraffin block of another melanoma as a control and stained with Sudan Black. The control melanoma was a heavily pigmented superficial spreading melanoma, also with a dominant (pigmented) nodule, with a Breslow thickness of 2.2 mm, 2 mitoses per mm^2, and no ulceration. Figure 7 is a composite image of both the melanoma reported here (upper image) and the control (lower image), both stained with Sudan Black. Both images are taken at with the same 4x objective and with identical exposure and white-balance settings. Apart from cropping and identical resizing for publication, there has been no photo manipulation. It can be seen that there is dif-

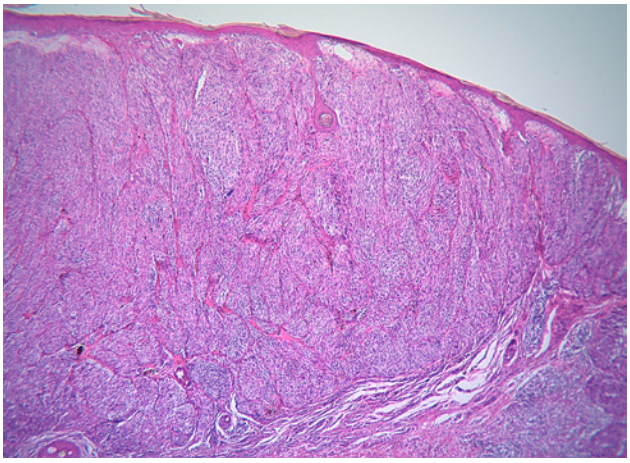

Figure 4. Medium high power dermatopathologic view of the lesion shown in Figure 3. Nesting is apparent at the base of the lesion. [Copyright: ©2014 Jegou Penouil et al.]

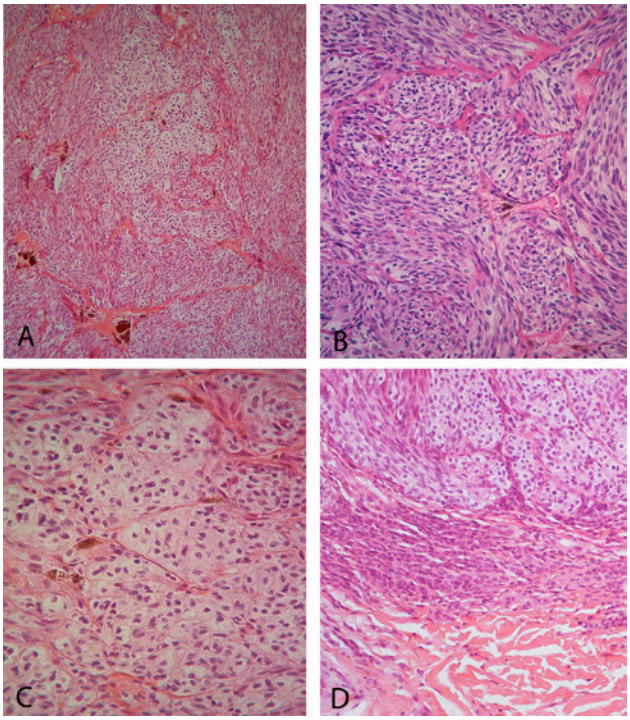

Figure 6. (A) Medium high power dermatopathologic view of the center of the lesion shown in Figure 3. Two distinct cell types are apparent, including spindle-shaped cells on one hand and cells with plump oval nuclei, prominent nucleoli and abundant clear cytoplasm (balloon cells) on the other. (B) High power view of spindle shaped cells and (C) balloon cells. (D) High power view of the base of the lesion shown in Figure 3. A sheet of mature nevomelanocytes can be seen beneath the nests of abnormal melanocytes, consistent with the contiguous presence of a nevus. [Copyright: ©2014 Jegou Penouil et al.]

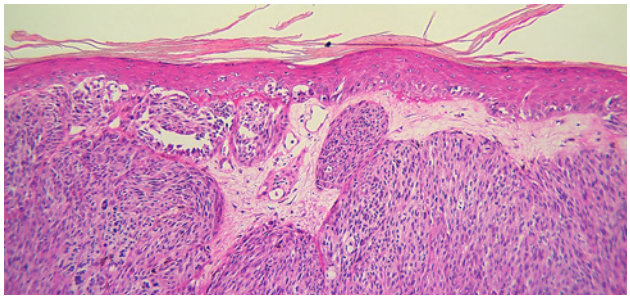

Figure 5. Higher power dermatopathologic view of the lesion shown in Figure 3 showing a proliferation of melanocytes at the dermoepidermal junction both as single cells and confluent nests with some clefting. A limited amount of pagetoid spread is seen. Sheets of spindle-shaped cells fill the dermis. [Copyright: ©2014 Jegou Penouil et al.]

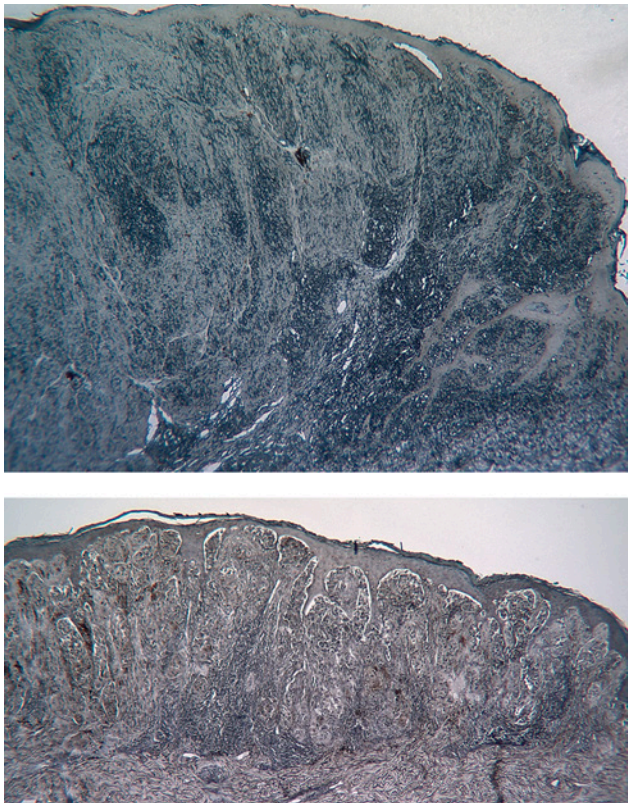

Figure 7. (Upper image) Dermatopathologic view of the lesion shown in Figure 3 stained with Sudan Black. (Lower image) Dermatopathologic image of a control melanoma of similar Breslow thickness and mitotic rate but with heavy melanin pigmentation. Both lesions had 5 micron thick sections stained with Sudan Black and the images were taken with the same exposure and white-balance settings. There has been no photo manipulation apart from cropping and identical resizing for publication. The case being reported here (upper image) is seen to stain differentially consistent with the possible presence of the pigment lipofuscin. [Copyright: ©2014 Jegou Penouil et al.]

ferential staining with Sudan Black in the upper image (case subject to this report) compared to the control.

Conclusions

While pigmented melanomas usually display dermatoscopic disorganization and clues related to their chaotic evolution [1], amelanotic/hypomelanotic melanomas (AHM) typically present with minimal clues due to melanin structures on which to base a diagnostic analysis [2]. The particular challenge, where a melanoma presents clinically as a hypomelanotic nodule, has been described as that of evaluating a rapidly enlarging *pink* tumor [3]. The melanoma reported here was a hypopigmented superficial spreading melanoma

(SSM) with a dominant nodule, which was notable because of its dominant structureless yellow color. In one series of four cases of AHM with dermatoscopic images, all cases had significant pink or red color and none had any yellow color [4]. Although this lesion fulfilled the definition of AHM, according to revised pattern analysis (RPA), the presence of any pigment should lead to a diagnostic analysis based on pigmented structures [5,6]. Applying the RPA algorithmic method for pigmented lesions, "Chaos and Clues" [1] this lesion was asymmetric by color and therefore was regarded as exhibiting chaos (defined as asymmetry of structure and/or color), and it had the clue of blue or gray structures so excision biopsy was indicated. In addition to these pigment clues, there were vascular dermatoscopic clues including an eccentric structurless pink area (Figure 2 upper pole) and a random arrangement of polymorphous vessels. Both milky red pink areas and linear irregular vessels are described as clues to AHM by Menzies et al. [7], and an eccentric structureless area (any color except skin color, including pink) and polymorphous vessels have been evaluated as clues to malignancy in RPA [8].

Dermatoscopic yellow color has also been attributed to keratin as seen in seborrheic keratosis [9] and congenital type nevus [10]. In a study of 400 BCCs Bellucci et al. found that 10% displayed yellow structures either as milia-like cysts (7.75%) or lobular structures (4.2%) [11], also presumably due to keratin. There was no accumulation of keratin to explain the yellow color in the melanoma reported here.

Structureless dermatoscopic yellow color has also been attributed to ulceration with surface serum exudate [6], and dermatoscopic structureless yellow color was described in the first case report of a balloon cell melanoma (BCM) with dermatoscopy [12], being attributed by the authors to ulceration. Considering the possibility that it may actually have been the balloon cells that caused the yellow color, the only other reported BSM with dermatoscopic images was a partially pigmented lesion with a dominant structureless white area and without any yellow color [13]. The case we report here did have two cell populations, including one with large cells with vacuolated cytoplasm resembling balloon cells (Figures 6 A, C, D), but it did not meet the criteria for diagnosis as a BCM which requires that the melanoma contain more than 50% of balloon cells, [14] and in fact the sheets of balloon cells were only present focally. With respect to ulceration as a reported cause of structureless yellow in one melanoma [12], there was no evidence of ulceration either clinically, dermatoscopically or dermatopathologically in the case reported here.

Another published cause of dermatoscopic yellow is the presence of sebaceous structures in sebaceous hyperplasia [15], nevus sebaceous and sebaceous adenoma [16]. Bryden et al. attributed the yellow color in sebaceous hyperplasia to sebum accumulation by proliferation of sebaceous glands [15]. Sebum consists primarily of a complex mixture of lipids [17]. Ideally staining for lipids is performed on fresh unfixed tissue with stains such as Oil Red O. In this case all tissue had been fixed in formalin and blocked in paraffin.

Subtle orange pigment, attributed to the pigment lipofuscin, a derived lipid which is an accumulation of lysosomes [18], is described as one of the features that can help differentiate choroidal melanoma from choroidal nevus [19]. The histochemical stain Sudan Black can be used on formalin-fixed, paraffin-processed tissue to detect some phospholids and also lipofuscin [18]. The melanoma reported here showed significant staining with Sudan Black compared to staining by a similar but deeply pigmented melanoma. This increased staining was present in varying intensity and uneven distribution throughout the dermal component of the melanoma consistent with the uneven presence of dermatoscopic structureless yellow (Figure 2).

The possible presence of the pigment lipofuscin in this melanoma is supported by positive staining by Sudan Black, and we speculate that the structureless yellow color displayed clinically and dermatoscopically may be due to the pigment lipofuscin, a pigment which has been previously described as a clue to choroidal melanoma.

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