

When algorithms falter: a case report of a very small melanoma excised due to the dermatoscopic “ugly duckling” sign

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ABSTRACT We present a case report of a 3.5 mm diameter superficial spreading melanoma on the upper back of a 27-year-old woman, signed out as Clark level 2, Breslow thickness 0.2 mm with regression to 0.45 mm. The patient, with Fitzpatrick type 1 skin and minimal actinic damage, had presented for a routine skin check with no previous history of skin cancers. At the age of 17 she had received chemotherapy and radiotherapy for Ewing’s sarcoma of the right hip with pulmonary metastases. The skin lesion was assessed as dermatoscopically symmetrical and was not predicted as a melanoma by any algorithmic method. The provisional diagnosis of melanoma was made on the basis that this lesion was completely different in dermatoscopic pattern to her other nevi, a dermatoscopic “ugly duckling” lesion. We draw attention to the recently established link between defects in the STAG2 gene and Ewing’s sarcoma, glioblastoma and melanoma.

Introduction

Small melanomas (diameter < 4 mm) present diagnostic difficulties, as the clinical and dermatoscopic characteristics of such lesions have been reported only rarely [1]. Another recent case report by Pellizzari et al suggests that in very small lesions chaos (asymmetry of structure or color) may not be unequivocally present [2]. This particular melanoma had the

diagnostic clue of lines radial, but as with the smallest published invasive melanoma [2], the radial lines were distributed circumferentially and any asymmetry was equivocal.

Case report

A 27-year-old woman presented for a routine skin cancer check in a primary care skin cancer clinic in Melbourne, Aus-

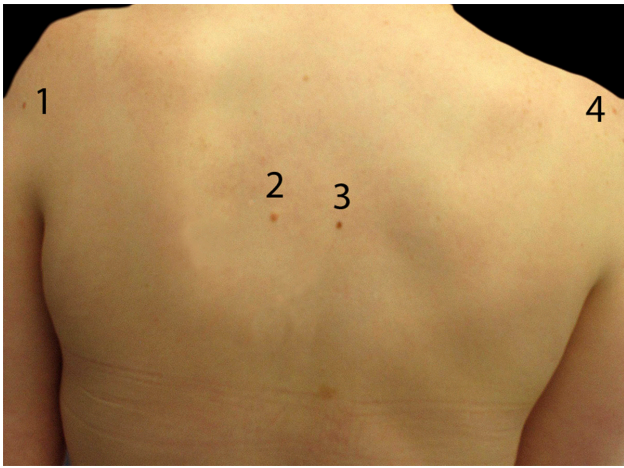


Figure 1. Clinical image of the back of a 27-year-old patient with Fitzpatrick type 1 skin and minimal actinic damage to the skin. Pigmented skin lesions (PSL) on both shoulders and at left para-thoracic location are macroscopically similar and were regarded as “signature nevi.” A PSL at the right para-thoracic location appeared different (darker) on clinical view. [Copyright: ©2013 Inskip et al.]



Figure 3. Dermatoscopy image of a pigmented skin lesion at the right para-thoracic location. This lightly pigmented brown lesion had a structureless pattern centrally combined with a circumferential pattern of radial lines peripherally, and as this differed markedly from the other “signature nevi” on the patient’s skin, it was regarded as a dermatoscopic “ugly duckling.” [Copyright: ©2013 Inskip et al.]

tralia. There was no family or personal history of melanoma or non-melanoma skin cancers. This was her first skin cancer screening examination and she had no concerns about any particular lesions on her skin. There was no history of excessive occupational or recreational sun or other ultraviolet light exposure and, specifically, she had never used solariums or welding equipment.

At the age of 17 she had been diagnosed with Ewing’s sarcoma of the right hip with pulmonary metastases and was treated with chemotherapy and radiotherapy for approximately one year. She remains under regular surveillance by a consultant oncologist.

On examination the patient had Fitzpatrick skin type 1 but only mild actinic damage, with small ephelides of the nasal bridge, upper medial cheeks and on the shoulders. Only seven other pigmented skin lesions (presumed melanocytic) were discovered on her skin. All lesions were examined

with a Heine Delta® 20 non-polarizing dermatoscope (Heine Optotechnik, Herrsching, Germany) at 10x magnification. Digital clinical and dermatoscopic photographs were taken with a Medicam 800 Fotofinder® non-polarized camera (FotoFinder Systems GmbH, Aichner, Birnbach, Germany), the dermatoscopy images at 20x magnification (Figures 1-3).

Of the seven presumed melanocytic, pigmented lesions, there were six which all had similar clinical and dermatoscopic features. They were each lightly pigmented with a structureless brown pattern and with a vascular pattern of curved vessels. These six lesions were assessed as being consistent with dermal nevi and were designated as “signature nevi” [3] for this patient. The seventh lesion was located on the right para-thoracic location, and it was slightly different to the other six lesions on naked eye examination, being darker, but it was markedly different by dermatoscopic assessment. The maximum diameter of this pigmented lesion

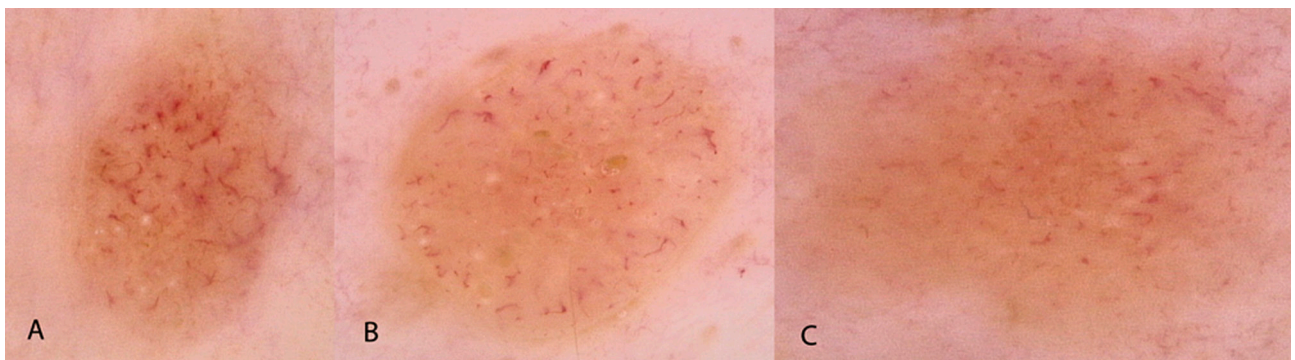


Figure 2. Dermatoscopic images of three pigmented lesions on the patient in Figure 1: (A) left shoulder, (B) left para-thoracic, and (C) right shoulder. Each of these lightly pigmented lesions has a structureless pattern and clues to dermal nevi of curved vessels, and in the case of A and B, white clods. These were regarded as “signature nevi” and were similar to three other pigmented skin lesions discovered on the patient’s skin. [Copyright: ©2013 Inskip et al.]

was 3.5 mm, measured with the dermatoscope footplate scale. This lightly pigmented brown lesion had a structureless pattern centrally combined with a circumferential pattern of radial lines peripherally. This was arguably a symmetrical pattern, taking into account that perfect symmetry is rare in biological material, and although radial lines are regarded as a clue to malignancy by a number of published algorithms [4,5,6,7], this lesion failed to reach the threshold for excision with respect to any algorithm which had a clearly defined flowchart method of predicting malignancy [5,6,7,8,9,10]. The treating clinician made the decision to excise this lesion because of its having a distinctly different dermatoscopic pattern to the signature nevi; he regarded it as a dermatoscopic “ugly duckling.”

Histology

Histology showed an asymmetric lentiginous proliferation of atypical epithelioid melanocytes along the dermoepidermal junction, with extension around the outer root sheaths of follicular infundibula and limited pagetoid intraepithelial scatter (Figures 4 and 5). Focal junctional nesting was present. There was one nest of atypical melanocytes in the papillary dermis at a depth of 0.2 mm associated with an eccrine duct. The atypical cells were angulated, with hyperchromatic pleomorphic nuclei and dusty brown cytoplasm. There was chronic inflammation, fibrosis and pigment incontinence, suggesting regression. There was no evidence of ulceration, lymphovascular invasion or satellitosis. The overall features were regarded by the reporting pathologist (author JM) as early level II malignant melanoma of superficial spreading type; thickness 0.2 mm and author DW concurred, although both authors did not rule out the possibility that this nest was connected to the epidermis of the eccrine duct, this possibly being obscured in the section seen.

Discussion

A review published in 2004 found that small melanomas (<6 mm so not conforming to the ABCD criteria where D stands for D = diameter of 6 mm or more) make up less than 1 to 38% of all invasive melanomas [11]. It has previously been reported that small melanomas may not be asymmetrical [1,2]. It has also been reported that hyperpigmentation was the defining feature in all of 13 small melanomas (<4 mm diameter) in one series of 95 melanomas [12], but Pellizzari et al pointed out that this may in fact be due to selection bias,

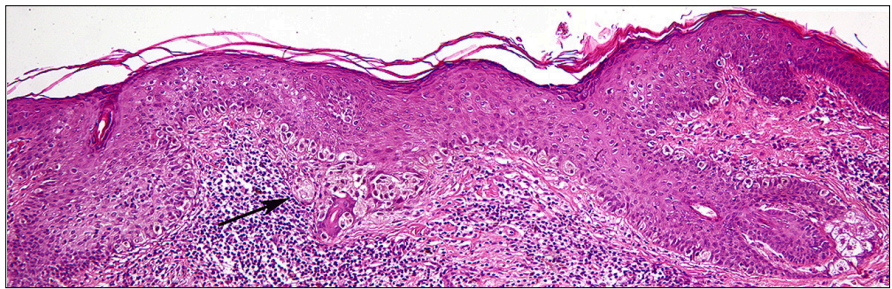


Figure 4. Scanning power photomicrograph of the lesion shown in Figure 3. There is a lentiginous array of atypical melanocytes at the dermoepidermal junction with some confluence and partial thickness pagetoid spread. Centrally there is involvement of a terminal eccrine duct with a nest of atypical melanocytes in the dermis adjacent to that (arrow). On the right side of the image there is involvement of a follicle by the melanocytic proliferation. [Copyright: ©2013 Inskip et al.]

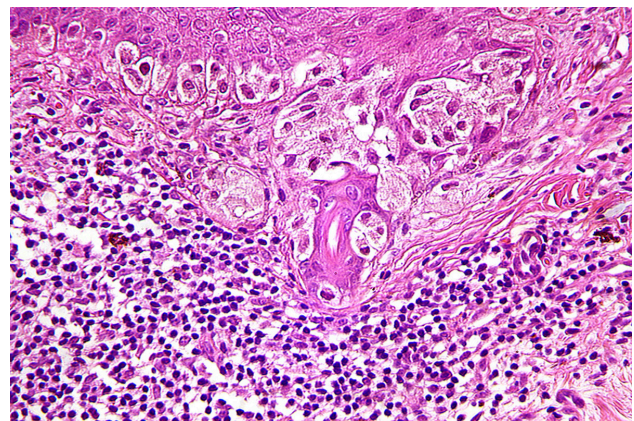


Figure 5. High power photomicrograph of the involved eccrine duct and adjacent dermal nest of atypical melanocytes shown in Figure 4. A brisk lymphocytic infiltrate is evident in the dermis. [Copyright: ©2013 Inskip et al.]

with darker lesions being discovered, while paler, hypomelanotic lesions may not be suspected at the stage where they are very small [2].

The clinician excised this lesion not because malignancy was predicted by any algorithm, but because in his opinion it was a dermatoscopic “ugly duckling.” The “ugly duckling” sign was proposed as a useful clinical tool to increase specificity in contrast to the clinical ABCD algorithm [13]. One small study evaluated the “ugly duckling” sign as a dermatoscopic clue and found that in most patients, 80% or more of their nevi could be grouped into one, two or three dermatoscopic patterns [14], although there were no melanomas included in the studied lesions.

The melanoma described in this report occurred on type 1 skin but there was no history to suggest excessive exposure to UV radiation. UV exposure is a causative factor for melanoma [15], but it is also known that exposure to electromagnetic radiation in cancer therapy can increase the risk of cutaneous malignancy, including melanoma [16]. In one study by Inskip et al., in the study cohort of childhood cancer survivors that received radiotherapy, eight developed malignant melanomas, whereas only 3.1 were expected sta-

tistically [17]. Radiotherapy may be an etiological factor in this case with a history of the patient having been treated for Ewing's sarcoma with pulmonary metastases ten years earlier. It is recommended that survivors of childhood cancer have systematic ongoing surveillance for sequelae of their therapy, including their risk of melanoma [18].

Although this lesion was signed out as an invasive melanoma, the reporting pathologist conceded that invasive status was equivocal. In such circumstances it is appropriate to render a report of invasive status, as this will determine surgical margins, which will default to the more significant option.

There is a recently established genetic link between Ewing's sarcoma, melanoma and glioblastoma. Researchers at Georgetown School of Medicine, Washington, USA, have found defective copies of STAG2 gene in 21% of Ewing's sarcoma, 19% of melanoma and 19% of glioblastoma [19]. The possibility of a genetic link between the preceding Ewing's sarcoma and the subsequent melanoma in this case is speculative but mentioned.

Conclusion

Small melanomas (<6 mm diameter) will not be predicted by the clinical ABCD rule and they may not be predicted by currently published dermatoscopic algorithms. This particular lesion was not diagnosable by any of the published algorithms for pigmented skin malignancy. A correct provisional diagnosis was made purely by application of the "ugly duckling" sign applied on the basis of dermatoscopic pattern; i.e., the suspect lesion was markedly different on dermatoscopic examination to all the patient's other "signature nevi." This case supports the assertion by Pellizzari et al that very small melanomas may not have had sufficient time to develop unequivocal asymmetry. It also highlights the importance of skin surveillance where there is a history of radiotherapy, and it draws attention to the possibility that different tumor types may be genetically linked.

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