Epidermotropic metastatic melanoma
A diagnostic challenge in a 25 year old man

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Introduction

- Epidermotropic metastatic melanoma (EDMM) is rare and histopathology alone cannot reliably distinguish EDMM from primary melanoma

Case Report

- A 25-year-old Caucasian man referred for skin surveillance after developing his second primary melanoma on the right thigh (Stage III-A) seven years after his first primary melanoma on the left flank (sentinel lymph node biopsy negative). He completed 12 months of adjuvant immunotherapy with nivolumab (anti-PD-1) without toxicity.

- Over the subsequent two years, including whilst on immunotherapy, nine new cutaneous nodules over his scalp, trunk and limbs were identified in conjunction with total-body-photography (TBP).

- Histopathology demonstrated melanomas with atypical epithelioid cytomorphology with no to variable epidermal involvement. Wide local excisions were performed. Germline testing was negative for CDKN2A mutation.

- Targeted molecular mutational profiling using Next Generation Sequencing (ArcherDx®) on 4 different cutaneous melanomas from the preceding two years was performed. These showed the same TERT-promoter and BRAFV600E mutation which supported a scenario of clonality and diagnosis of EDMM.

- Targeted therapy (dabrafenib and trametinib) was commenced and bridged to ipilimumab(anti-CTLA-4) and nivolumab.

- No new EDMM developed whilst on treatment however was interrupted due to hepatitis and colitis followed by progressive disease with additional EDMM, intracranial and leptomeningeal metastases (Stage IV,M1d).

Figure 1: Molecular Targeted Analysis – clonality demonstrated

Date	Site	Molecular	
Sept 2020	R Scalp	TERT promoter region chr5;1295250 C->T	BRAF V600E chr7;140453136 A->T
July 2021	R Scalp	TERT promoter region chr5;1295250 C->T	BRAF V600E chr7;140453136 A->T
April 2022	R Flank	TERT promoter region chr5;1295250 C->T	BRAF V600E chr7;140453136 A->T
April 2022	Back	TERT promoter region chr5;1295250 C->T	BRAF V600E chr7;140453136 A->T

Discussion

- This case demonstrates a multidisciplinary approach to distinguish EDMM from primary melanomas and its implications on staging, treatment and prognosis.

- Histology alone may not be sufficient to establish a diagnosis therefore clinicopathological correlation is required.

- Demonstration of clonality with molecular techniques may support a diagnosis of EDMM while TBP could assist in monitoring for new or evolving lesions.[1]

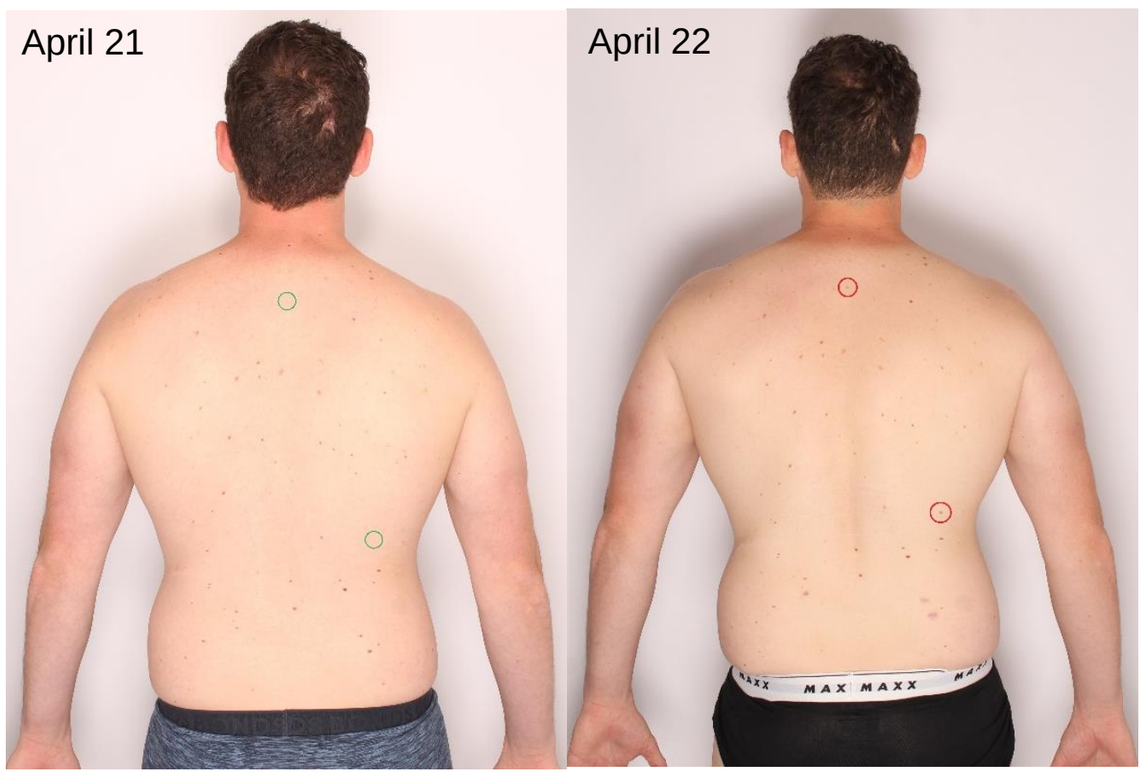

Figure 2: Total Body Photography comparisons – new lesions in red

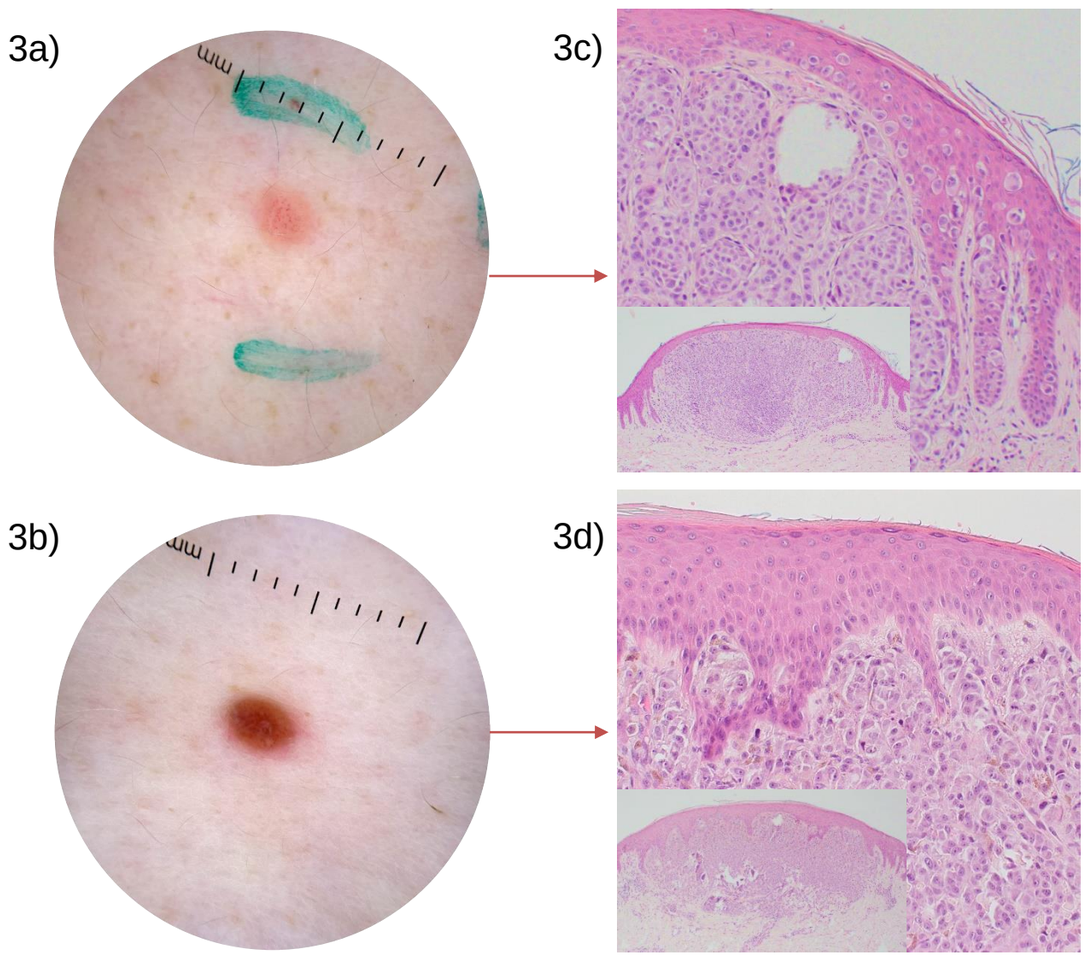

Figure 3a, 3b:
Dermoscopy – New pink and brown nodules

Figure 3c, 3d:
Histopathology shows the predominantly dermal based deposits of melanoma, with matching atypical epithelioid cytomorphology, with the melanoma in 3c showing eccentric focal upward and pagetoid spread.

References

1. Skala SL et. al. Comprehensive histopathological comparison of epidermotropic/dermal metastatic melanoma and primary nodular melanoma. Histopathology. 2018 Feb;72(3):472-480. doi: 10.1111/his.13384. Epub 2017 Nov 21. PMID: 28881040.