The dilemma of whether to continue TNF α blocker therapy in an ulcerative colitis patient newly diagnosed with a malignant melanoma and melanoma in situ

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DESCRIPTION

Our case concerns a 75-year-old Caucasian woman with Fitzpatrick type 1 skin who presented to our department with a 6 mm irregularly shaped pigmented lesion on her right upper back. Full skin examination revealed a 1 cm irregularly shaped melanocytic lesion on her left calf ([figure 1](#)). She has a history of ulcerative colitis (UC) managed with an adalimumab biosimilar 2 months prior to presentation; previous to this she had received adalimumab (Humira) for 4 months. Other treatments she has previously received for her UC included prednisolone and mesalazine only. The right upper back lesion was excised revealing a superficial spreading malignant melanoma (figure 2A,B; pT1b, Breslow thickness 0.8 mm; Clark level III; clinical stage 1a). Subsequent 1 cm wide local excision revealed scar tissue only. The left calf lesion revealed melanoma in situ (figure 2C,D) excised with 5 mm radial margin.

Adalimumab is a fully human recombinant IgG1 monoclonal cytokine of the innate immune system that blocks tumour necrosis factor alpha (TNF α), which in turn plays a key role in the surveillance of malignancies. Our manuscript reviewer helpfully highlighted the current literature reported different perspectives on the melanoma risks of patients on TNF α blockers: neutral, with or against the theory. There were case reports associating TNF α blockers with an increased risk of developing melanoma (Crohn's disease and adalimumab¹; psoriasis and adalimumab² or recurrence of malignant melanoma (rheumatoid arthritis and adalimumab).³ Long *et al* reported a number of inflammatory bowel disease (IBD) patients on TNF α blockers

Figure 2 Lesion right mid back (A,B) showing a superficial spreading malignant melanoma, vertical growth phase, Breslow 0.8 mm (H&E 100 $\times$ and H&E 200 $\times$). Lesion left calf (C,D) interpreted as a partly nested but widely lentiginous mildly atypical melanocytic proliferation with some pagetoid ascent favouring melanoma in situ (H&E 50 $\times$ and H&E 40 $\times$). The irregularity of the junctional nesting and the extent of lentiginous and pagetoid spread are highlighted by the associated immunostaining panels (MelanA at 50 $\times$ and 200 $\times$).

developed a melanoma.⁴ They postulated the potential mechanism for this could include melanomas developing in the condition of immunosuppression, or de novo lesions developing secondary to increasing photosensitivity. Conversely, a systematic review by Singh *et al* demonstrated an increased risk of melanoma in IBD patients independent of biological treatment, thereby encouraging clinicians to warn patients of this risk irrespective of their intended treatments.⁵ Therefore, highlighting the importance of long-term skin surveillance in this patient population. The patient was counselled about the association between TNF α blocker and melanoma risks including our findings from the literature as stated above. Guided by patient choice, and in conjunction with the gastroenterology and dermatology teams, she continued on adalimumab biosimilar treatment while undergoing long-term skin surveillance. We advocate that patient education when starting biologics, as well as in at risk groups such as IBD patients, through regular skin surveillance and reduced sun exposure may help to identify early melanomas. Continued long-term data acquisition through biological registries will

Figure 1 (A) An asymmetrical irregular-shaped variegated colour melanocytic lesion located on the patient's left calf. (B) The dermoscopy view of the asymmetrical melanocytic lesion with atypical networks and globules.

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also help to further appraise risks in such treatment groups. Treatment choices in patients with IBD and melanoma are challenging, and there are limited data available to help guide management. Treatment and follow-up should therefore be individualised, extensively discussed with patients and their families as appropriate, and done in conjunction with close follow-up by gastroenterologist and dermatologist.

Learning points

- ▶ The literature reported an association between melanoma and inflammatory bowel disease.
- ▶ The literature also reported an association between melanoma and tumour necrosis factor alpha blockers.
- ▶ Patient education when starting biologics, as well as in at risk groups such as inflammatory bowel disease patients, through regular skin surveillance and reduced sun exposure may help to identify early melanomas.

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