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Commentary – Tumor necrosis factor-α antagonists as therapies for vitiligo

Vitiligo is a common cutaneous disease resulting from the loss of epidermal melanocytes.[1] Although the aetiology and pathogenesis of vitiligo are not completely understood, cytotoxic T cell responses against melanocytes clearly play a prominent role in the pathophysiology of the disease.[2] In addition, an imbalance of cytokines within vitiligo-affected skin has been implicated in the destruction of melanocytes.[3] For example, epidermal levels of the proinflammatory cytokine tumor necrosis factor (TNF)-α are increased in vitiligo skin and, indeed, correlate directly with on-going depigmentation.[4] TNF-α can activate cytotoxic T cells in the skin,[5] inhibit the proliferation of melanocytes[6] and also cause melanocytes to apoptose.[7] Such findings have prompted the investigation of TNF-α inhibitors as agents that may prevent melanocyte loss and also initiate repigmentation in vitiligo patients.

In this issue of the *BJD*, Webb *et al*[8] have reviewed the literature pertaining to the use of anti-TNF-α mediators such as infliximab, etanercept and adalimumab as therapeutic tools for vitiligo. Their findings revealed that blocking the action of TNF-α effectively stopped the progression of vitiligo and initiated repigmentation in almost all patients with active disease, presumably at least in part due to the stemming of cytotoxic T cell-mediated destruction of melanocytes. Importantly, the researchers noted that the arrest of melanocyte loss was as valid in assessing the success of treatment as observing actual repigmentation, concluding that future clinical trials will need to effectively evaluate both parameters.

Interestingly, the literature reported a small proportion of non-vitiligo patients who were receiving treatment with TNF-α antagonists adalimumab and infliximab for other autoimmune diseases and who developed depigmentation. The authors of the review suggest that this phenomenon results from a decrease in the production and activation of regulatory T cells (Tregs) which are normally stimulated by TNF-α[9] and act to supress cytotoxic T cell activity.[10] If Treg cell numbers are reduced in the skin, then T lymphocytes cytotoxic to melanocytes may exert their effects leading to pigment cell loss. Simultaneous treatment to recruit Tregs to the epidermis may overcome this adversity in susceptible individuals.

Overall, inhibitors of TNF-α were found to be beneficial for patients with progressing vitiligo. However, the possibility that vitiligo can be initiated by TNF-α antagonists may thwart their wider use as treatments for the disease.

Conflicts of interest

None declared.

DR. E. HELEN KEMP

Department of Human Metabolism

University of Sheffield

Sheffield S10 2RX

U.K.

Email – e.h.kemp@sheffield.ac.uk

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