Title	Repigmentation of vitiligo with oral baricitinib
Running Title	Repigmentation vitiligo baricitinib
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Article type : Case Letter

We report a case of vitiligo repigmenting after the patient was prescribed oral baricitinib, a new Janus kinase (JAK) inhibitor, for his concurrent rheumatoid arthritis.

A 67-year-old Caucasian male was referred with vitiligo affecting the hands and forearms which he first noticed in July 2018. His only significant medical comorbidity was rheumatoid arthritis, diagnosed in 2008 which predominantly affected the small joints of the hands and feet. Rheumatoid factor and anti-citrullinated protein antibodies were strongly positive. Anti-nuclear antibodies were present with a titre of 1:80, and anti-dsDNA antibodies were undetectable. Full blood count, renal function, and liver function tests were unremarkable. No histopathology was performed.

Previous treatments for his rheumatoid arthritis included methotrexate, prednisolone, leflunomide, tocilizumab, golimumab, and adalimumab. No previous topical or systemic treatment had been commenced specifically for vitiligo.

In August 2018, three weeks after developing vitiligo, oral tofacitinib 5mg BD was commenced as monotherapy for the treatment of his rheumatoid arthritis. Whilst taking tofacitinib he noticed no significant improvement in depigmentation. In January 2019, tofacitinib was substituted for baricitinib 4mg daily to reduce pill burden via daily dosing. At follow up eight months after the commencement of baricitinib, almost complete repigmentation of the hands and forearms was observed (Fig. 1 and 2). Treatment with both JAK inhibitors was well tolerated with no adverse effects.

Interferon gamma (IFN-γ) and the associated chemokine CXCL-10 are implicated in the pathogenesis of vitiligo and seem to maintain an active inflammatory process which destroys melanocytes [1]. IFN-γ signalling is mediated by the Janus kinase-signal transducer and activator of transcription (JAK-STAT)

pathway, specifically via JAK1 and JAK2 [2]. JAK inhibitors can block this pathway and consequently the actions of IFN-γ and CXCL-10 [3].

Tofacitinib and ruxolitinib are first generation JAK inhibitors which inhibit JAK1/3 and JAK1/2 respectively [4]. Both of these agents can effect significant repigmentation in patients with vitiligo and response to treatment is usually observed rapidly [5]. However, concomitant stimulation of melanocytes via skin exposure to ultraviolet light appears to be required to achieve repigmentation [2].

To our knowledge this is the first published case of vitiligo responding to baricitinib. Baricitinib has recently been approved for the treatment of rheumatoid arthritis in Australia and differs from tofacitinib in that it preferentially inhibits JAK1/2 rather than JAK 3 [4]. Given IFN-γ is mediated via JAK1/2, it has been suggested that JAK inhibitors which predominantly inhibit these JAKs may be more effective than others [2].

In this case treatment with tofacitinib for a period of six months did not result in repigmentation, suggesting that substitution with a different JAK inhibitor may be a viable strategy in refractory cases of vitiligo.

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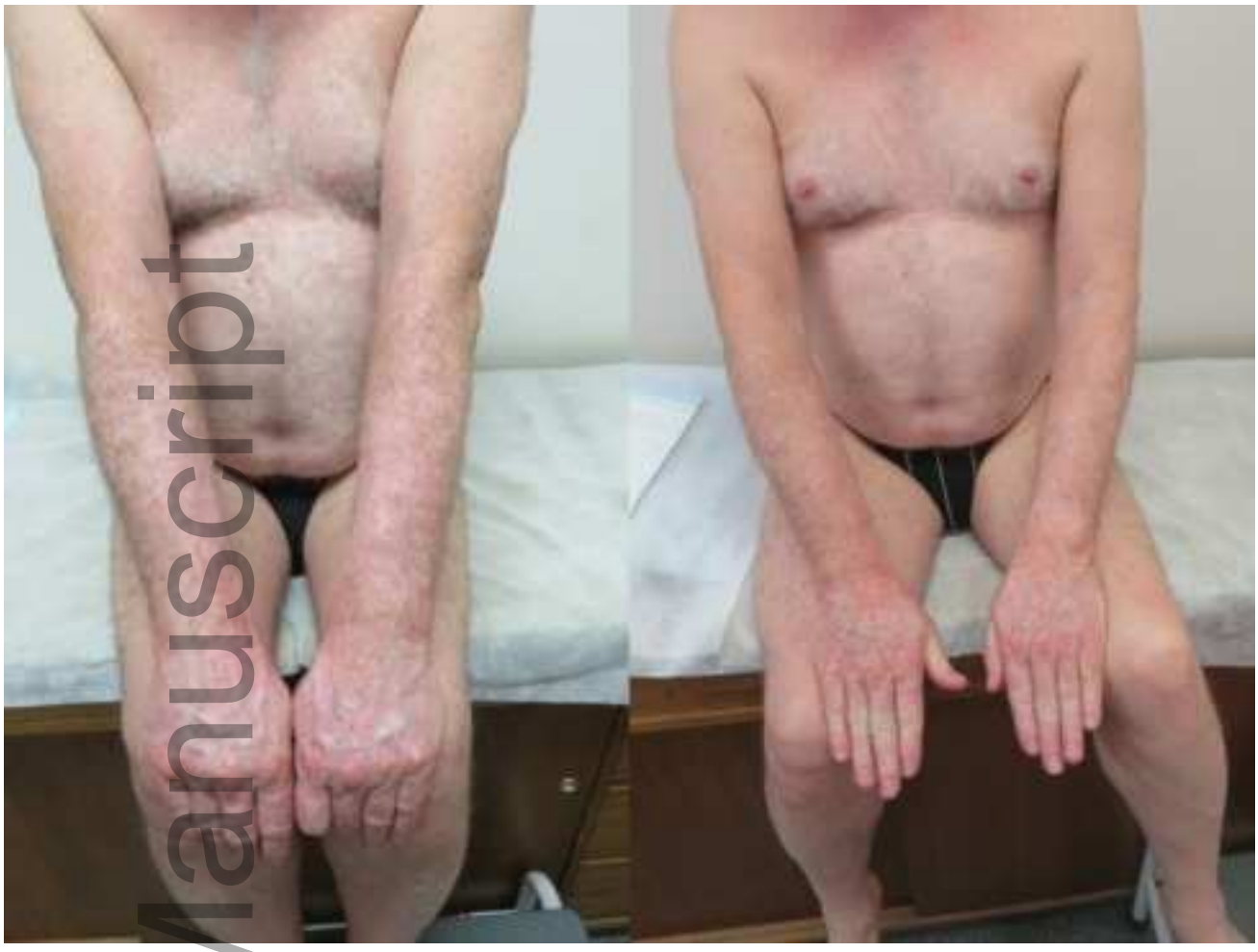

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