Ruxolitinib cream for the treatment of cutaneous sarcoidosis

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Key words: cutaneous sarcoidosis; JAK inhibitors; ruxolitinib.

CASE REPORT

A 66-year-old woman with a history of multisystem sarcoidosis, with lung, pericardial, and skin involvement, presented to the dermatology clinic with an indurated pink plaque on the left side of her forehead for a duration of 2 months. In this clinical context, her lesion was consistent with prior biopsy-proven cutaneous sarcoidosis. Her systemic sarcoidosis was well controlled with 10-mg/kg infusions of infliximab every 4 weeks and methotrexate 25 mg administered subcutaneously weekly. However, the patient continued to experience flares of recalcitrant cutaneous disease. Her forehead lesion was refractory to low-potency topical steroids and intralesional triamcinolone acetonide at 5 mg/mL, in addition to her infliximab and methotrexate. The patient was also concerned about steroid-induced skin atrophy with continued treatments of intralesional triamcinolone acetonide or high-potency topical steroids in a cosmetically sensitive area. We extensively reviewed other options, including additional systemic agents, but we determined the potential safety and tolerability burden to be unacceptably high. We recommended a steroid-sparing topical agent; however, topical tacrolimus could not be obtained through the patient's insurance. Reports of oral Janus kinase (JAK) inhibition with tofacitinib to treat patients with systemic and cutaneous sarcoidosis were published, one in the *New England Journal of Medicine* with demonstration of clinical and molecular improvement.[1,2] Reports of topical JAK inhibition with tofacitinib to treat cutaneous sarcoidosis have also demonstrated clinical improvement.[3,4] Given the potential safety challenges of systemic JAK inhibition, especially in combination with other immunosuppressive medications, and the benefits of JAK inhibition in sarcoidosis, we prescribed ruxolitinib 1.5% cream.[5] Her forehead lesion completely resolved without residual stigmata within 6 weeks of twice daily application (Fig 1).

Abbreviations used:

JAK: Janus kinase
STAT: signal transducer and activators of transcription

DISCUSSION

The JAK–signal transducer and activators of transcription (STAT) signaling pathway, whereby interferon gamma activates JAK1 and JAK2, in turn activating STAT1, is known to play a role in the pathogenesis of sarcoidosis.[3] There is also histopathologic evidence of STAT1 and STAT3 activation in skin with active cutaneous sarcoidosis.[1] Ruxolitinib blocks JAK1 and JAK2.[3] To our knowledge, this is the first report of improvement of cutaneous sarcoidosis by topical ruxolitinib, providing further support for using topical JAK inhibitors in the treatment of cutaneous sarcoidosis. It is possible that similar efficacy will be observed in other cutaneous granulomatous processes, although additional studies are needed to test this hypothesis. Our case suggests that, in certain diseases, topical JAK inhibitors may provide similar cutaneous benefit with an improved safety profile relative to oral therapy.[5]

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Funding sources: None.

IRB approval status: Not applicable.

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JAAD Case Reports 2023;38:111-2.

2352-5126

https://doi.org/10.1016/j.jdcr.2023.05.032

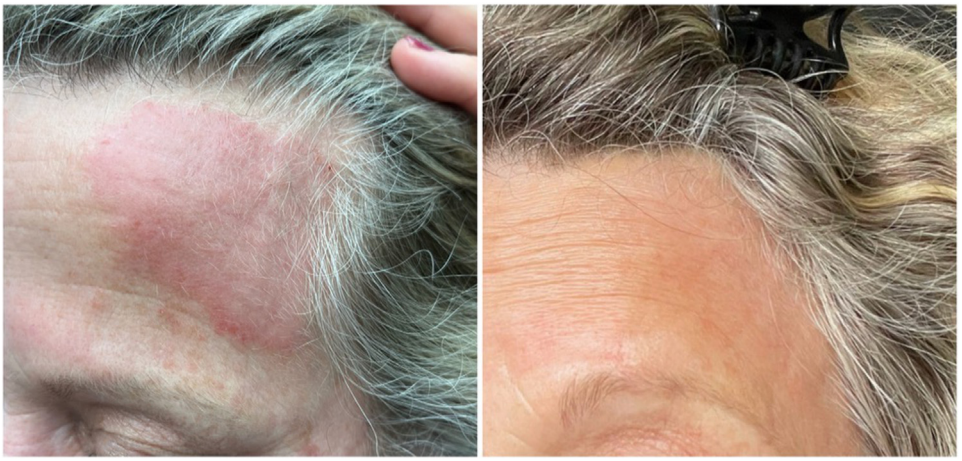

Fig 1. Cutaneous sarcoidosis response to ruxolitinib cream. The *left photo* shows a recalcitrant indurated pink plaque of cutaneous sarcoidosis before treatment with ruxolitinib 1.5% cream. The *right photo* shows resolution of the plaque after 6 weeks of treatment.

Conflicts of interest

Dr Merola is a consultant and/or investigator for Merck, AbbVie, Dermavant, Eli Lilly, Novartis, Janssen, UCB, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Serono, Avotres, and Leo Pharma. Dr Smith and author Woodbury have no conflicts of interest to declare.

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