SHORT COMMUNICATION

Unexpected Hair Regrowth in a Patient with Longstanding Alopecia Universalis During Treatment of Recalcitrant Dermatomyositis with the Janus Kinase Inhibitor Ruxolitinib

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This case report describes the successful treatment of a woman with refractory dermatomyositis (DM) with ruxolitinib, a specific janus kinase (JAK) inhibitor, which concomitantly resulted in complete remission of her longstanding alopecia areata universalis (AA).

CASE REPORT

A woman in her 40s presented at our department with an acute exacerbation of a recalcitrant DM first diagnosed 6 years ago. She reported severe weakness of proximal muscles of the extremities, which left her incapable of coping with everyday business. Clinical examination revealed DM-typical skin symptoms, such as a heliotropic erythema at her peri-orbital area, her chest (“v-sign”) and neck (“shawl-sign”), as well as erythro-squamous papules on the dorsal side of the finger joints (“Gottron’s sign”). Her laboratory results revealed antinuclear antibodies (ANA) in high titres and transcriptional intermediary factor 1 (TIF1-γ) antibodies. Treatment attempts with prednisolone, azathioprine, methotrexate, etanercept, intravenous immunoglobulins, rituximab, hydroxychloroquine, cyclosporine A, mycophenolate mofetil and cyclophosphamide remained ineffective or had to be discontinued because of drug-related side effects. (Table I).

The patient had also had AA for more than 20 years, and despite the aforementioned immunosuppressive drugs, she presented clinically with complete baldness of the scalp during the last 10 years. Due to the ineffectiveness of the numerous previous treatment strategies it was decided to start steroid-pulse therapy (1,000 mg prednisolone/day on 3 days per month, for 3 consecutive months), which reduced creatine kinase (CK)-serum levels, but left the patient in a poor general condition and with a strong myalgia, muscle strength and skin condition. In addition, the patient showed generalized hair regrowth on the scalp and eyebrows (Fig. 1A). To date, both DM and AA have remained significantly improved under monotherapy with ruxolitinib (30 mg per day).

DISCUSSION

JAK inhibitors have the potential to simultaneously target various pathogenic pathways by blocking intracellular signalling linked to a broad spectrum of receptors. Most importantly, these drugs are highly effective suppressors of proinflammatory cytokines, which function as key drivers in several autoimmune skin disorders, including DM, lupus erythematosus and AA (2). These diseases share a significant upregulation of interferon (IFN)-associated proinflammatory chemokine expression, which is mediated by JAK/signal transducers and activators of transcription (JAK/STAT) signalling. In particular, CXCR3+ chemokines are known to recruit effector cells into lesional tissue, inducing myocyte and keratinocyte cell death in DM and loss of the hair follicle immune privilege with anagen arrest in AA (3, 4). Strikingly, in the current patient, hair growth re-occurred under JAK inhibitor treatment, despite the patient’s decade-long and therapy-resistant extensive AA with clinically observed complete absence of hair follicles, which normally makes a treatment response highly unlikely (5). This might be due to a specific positive effect of JAK inhibitors on reinduction of hair follicle progenitor cells and immune privilege. This suggestion is supported by recent findings of our group in a lupus-prone mouse model (TREX1−/−), in which treatment of hairless skin lesions with a topical JAK inhibitor resulted in hair growth and a strong upregulation of hair cell cycle associated genes (Fig. 1C) (6).

Table I. Synopsis of all attempted treatments the patient received from 2013 until 2019, which partly remained ineffective or had to be terminated due to drug-related side effects

| Treatment                                      | Duration of treatment | Reason for cessation                                           |
|------------------------------------------------|-----------------------|---------------------------------------------------------------|
| Prednisolone; 20–30 mg/day (up to 500 mg/day) | 03/2013–04/2018 (intermittent) | Varying success                                               |
| Azathioprine                                    | 03/2013–08/2013       | Ineffectiveness, leukopenia                                    |
| Methotrexate; Varying dose                      | 08/2013–06/2014       | Hepatopathy                                                   |
| Etanercept                                      | 10/2013–12/2013       | Skin reactions                                                |
| Intravenous immunoglobulins                    | 01/2014–02/2014       | Exacerbation of myalgia and rash                              |
| Rituximab; 4×750 mg i.v.                        | 02/2014               | Ineffectiveness                                               |
| Hydroxychloroquine                              | 05/2014–06/2014       | Drug intolerence                                              |
| 12/2016–01/2017                                 |                       |                                                               |
| Cyclosporine A                                  | 07/2014–12/2014       | Ineffectiveness                                               |
| Mycophenolate mofetil; Varying: 2–3 g/day       | 12/2014–12/2016       | Loss of efficacy                                              |
| Cyclophosphamide                                | 02/2018–04/2018       | Leukopenia and loss of efficacy                               |
| Prednisolone pulse therapy; 1,000 mg i.v./day   | 11/2018–01/2019 (on 3 continuous days/month) | Slight difficulties in breathing (but not discontinued) |
| Ruxolitinib; 2×10 mg/day, 30 mg/day (since 04/2019) | Since 02/2019         |                                                               |

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In summary, this case demonstrates a notable benefit from JAK inhibitor treatment in a patient with both recalcitrant DM and AA. This case supports the idea of JAK inhibitors targeting shared central pathobiological features of these conditions in a specific manner compared with conventional immunomodulating drugs; thus providing an effective therapeutic strategy, particularly in refractory cases.

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