Ruxolitinib-induced reversal of alopecia universalis in a patient with essential thrombocythemia

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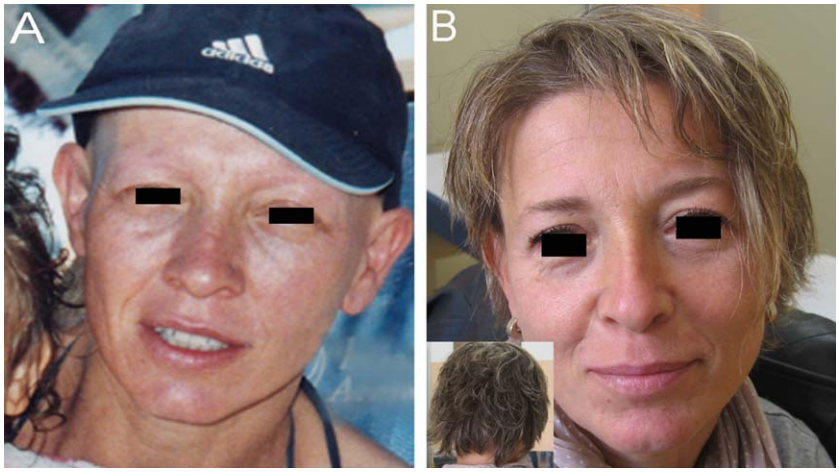

Image 1. Image in Panel A was taken from the 2007 family album depicting the patient on the beach with her 3-year old daughter (on the left). She was used to wear a hat in any occasion when outside home as she felt much ashamed of the alopecia. However, it is possible to appreciate the hairless skull, eyelashes, and eyebrows. Panel B is a picture taken at the last clinic visit in September 2014 when we asked the patient the permission to take a photo for the purpose of this report. Resolution of alopecia universalis is manifest.

Ruxolitinib is an inhibitor of activated JAK1 and JAK2 approved for the treatment of patients with myelofibrosis [1]. Disregulated activation of Janus kinase/signal transducer and activator of transcription (JAK/STAT) signaling, caused by activating mutations of *JAK2*, myeloproliferative leukemia virus oncogene, the thrombopoietin receptor (*MPL*), and calreticulin (*CALR*), is implicated in the uncontrolled proliferation of hematopoietic progenitors and the generation of a proinflammatory reaction responsible for symptomatic burden [2]. Ruxolitinib is under scrutiny in other hematologic and solid malignances as well as in rheumatoid arthritis and psoriasis. Recent data suggest that the list of autoimmune disorders in which ruxolitinib may be efficacious should include alopecia areata (AA) [3]. It is assumed that the cytolytic damage to the hair follicle in AA is caused by autoreactive CD8+ T cells that expand and self-maintain through a cascade of cytokines including interferon gamma, interleukin-2 and -15; these cytokine's receptors signal through JAK1 and JAK2 (JAK1/JAK3 for interferon), therefore, they are inhibited by ruxolitinib [4]. Topical administration of ruxolitinib promoted a full coat of hair in a mouse model of AA, and three individuals with AA receiving 20 mg ruxolitinib twice daily exhibited near-complete hair regrowth within 3–5 months [3].

A 24-year old lady was diagnosed with essential thrombocythemia in 1992 because of sustained thrombocytosis (650×10^9/L) and consistent bone marrow biopsy. She remained untreated until 2006, when platelet count was $1{,}200 \times 10^9$/L and she complained of severe microvascular symptoms; at that time, she was found *JAK2*V617F mutated. We prescribed interferon-alpha, that was withdrawn soon for intolerance. She refused hydroxyurea and anagrelide on several occasions, notwithstanding severe complains. Finally, in 2009, she was enrolled in a phase II trial (NCT00726232) with ruxolitinib [5]; she is still on therapy at 15 mg twice daily after 71 months with control of platelet count, complete resolution of symptoms, and no side effects.

On March 2002, the patient had been diagnosed as suffering from AA, eventuating into alopecia universalis in 2006 with loss of eyelashes and eyebrows (Image 1A). Then, after 10 months of receiving ruxolitinib, she presented an undeniable improvement of alopecia with progressively

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extending areas of hair regrowth shortly leading to almost complete recovery, that is, durable at 50+ months (Image 1B). At the time of hair regrowth in the patient, we suspected an association with ruxolitinib administration, but could not substantiate it. After the seminal report of Xing et al., it is now clear that the remission of alopecia universalis was a highly desirable "side effect" of therapy in our patient receiving ruxolitinib for other reasons.

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