Amelioration of unstable vitiligo and normalization of thryroglobulin antibodies with oral tofacitinib

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Key words: Hashimoto thyroiditis; repigmentation; thyroid; tofacitinib; vitiligo.

INTRODUCTION

Vitiligo is a dermatological autoimmune disease with a pathogenesis that continues to evolve as new medical technologies emerge. Treatment methods reported in the literature include topical steroids, topical immunomodulators, topical anthralin, oral polypodium leucotomos extract, systemic steroids, tofacitinib, narrowband ultraviolet B, psoralen with ultraviolet A photochemotherapy, excimer laser, and transplantation therapy.[1,2] Vitiligo has been widely associated with other autoimmune disorders, such as thyroid disease, pernicious anemia, alopecia areata, and inflammatory bowel disease.[2,3] Therefore, testing for thyroid stimulating hormone (TSH), free thyroxine (FT4), thyroid peroxidase antibodies, thyroglobulin antibodies (TgAb), antinuclear antibodies, and antiparietal gastric cell antibodies can be ordered, when a high clinical suspicion exists for potential comorbidities.[2,4] These are yet to be used as markers of unstable vitiligo and treatment response.

Abbreviations used:

CXCL:	C-X-C motif chemokine ligand
FT4:	free thyroxine
TBSA:	total body surface area
TgAb:	thyroglobulin antibody
TSH:	thyroid stimulating hormone

CASE REPORT

A 56-year-old woman with a past medical history significant for "well-controlled" Hashimoto thyroiditis, presented with vitiligo affecting 30% total body surface area (TBSA) of the face, hands, arms, and neck. The patient was treated with alpha lipoic acid, vitamin C, vitamin E, polypodium leucotomos extract, and topical pimecrolimus 1% cream for 6 weeks before initiation of narrowband ultraviolet B (NBUVB) and excimer laser therapy. After the patient developed new lesions and confetti-like macules that expanded her TBSA from 30% to 35% despite therapy over the next 5 weeks, further testing was pursued to determine the cause of the unstable vitiligo.

Table I. Serum thyroglobulin antibody (TgAb) levels and clinical response to tofacitinib

Number of weeks from treatment initiation	TgAb levels (IU/mL)	TBSA vitiligo (%)	Tofacitinib dosage
−11	2	30	N/A
−5	3	35	N/A
0	3	35	5 mg twice daily
4	1	35	5 mg twice daily
8	NR	15	5 mg twice daily
10	NR	12	5 mg twice daily
19	NR	10	5 mg daily

TgAb, Thyroglobulin antibodies*; TBSA,* total body surface area.

The TgAb level was elevated at 3 IU/mL (reference range, ≤ 1 IU/mL), but both TSH and FT4 levels were within normal limits with the ongoing levothyroxine treatment. A test for antinuclear antibodies was negative. Prior laboratory tests from the patient's endocrinologist revealed a TgAb concentration of 2 IU/mL prior to vitiligo treatment and TSH and FT4 levels both within normal limits. Further examination of the patient revealed arthritis of

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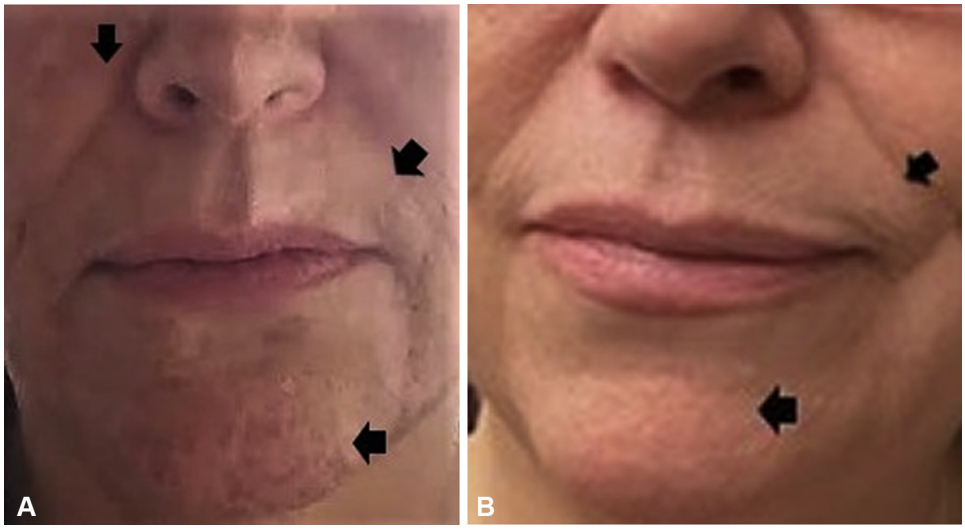

Fig 1. A, Vitiligo before addition of tofacitinib. **B,** Vitiligo after 19 weeks of tofacitinib therapy. Note repigmentation around lips and nose tip.

bilateral elbows and knees, diffuse nonscarring psoriatic alopecia, and psoriasis on the elbows.

Tofacitinib 5 mg twice daily was added to the treatment regimen. Within the first month of treatment with tofacitinib, the TgAb level normalized to 1 IU/mL, and clinical improvement in TBSA of vitiligo appeared shortly thereafter (Table I). At week 19, gastrointestinal side effects from the tofacitinib prompted a decrease in dosage from 5 mg twice daily to 5 mg once daily. By then, the TBSA of vitiligo had decreased to 12%, (Fig 1), alongside a resolution of the patient's arthritis and psoriasis and improvement in alopecia.

DISCUSSION

This case suggests that unstable vitiligo may be associated with elevated TgAb levels despite normal TSH and FT4 levels. The decrease in TgAb from 3 to 1 IU/mL is a statistically significant change for the TgAb assay from Quest Diagnostics. An elevated TgAb level is indicative of autoimmune thyroiditis but is not addressed by endocrinologists when TSH and FT4 levels are normalized by thyroid supplementation.[5] Consultation with several prominent endocrinologists confirmed that "treatment" of elevated levels of TgAb merely consists of increasing the levels of levothyroxine to normalize TSH and FT4 but that elevated levels of TgAb are otherwise ignored.

Because of its Food and Drug Administration-based approval for psoriatic arthritis and reports of effect on vitiligo,[6] tofacitinib 5 mg twice daily was initiated, with normalization of TgAb levels in 4 weeks and a decrease in TBSA from 35% to 15% over 8 weeks. As a Janus kinase inhibitor, tofacitinib may impact the pathogenesis of vitiligo through its impact on CD8+ T cells, interferon-gamma, and C-X-C motif chemokine ligand (CXCL) 10.[6-9] Recent studies correlate disease activity of vitiligo with the concentration of melanocyte-specific CD8+ T cells, interferon-gamma, and interferon-gamma-induced chemokines (CXCL9 and CXCL10) and postulate that serum CXCL10 may be a novel biomarker in monitoring disease activity in progressive vitiligo.[7,8] Similarly, Hashimoto thyroiditis and other autoimmune thyroid diseases have also been associated with functional polymorphisms and increases in CXCL10.[9]

This case report suggests that TgAb, even in the presence of normal levels of TSH and FT4, may be a useful biomarker in the detection of unstable vitiligo when clinically indicated. We propose that TgAb may be a more widely available biomarker than CXCL10 for clinical dermatologists for vitiligo disease activity in patients with unstable or progressive vitiligo. This case suggests that Janus kinase inhibitors may ameliorate vitiligo by impacting TgAb via effects on CXCL10 and cytotoxic T cells, which are overexpressed in both vitiligo and autoimmune thyroiditis, and may preserve thyroid function. With the recent approval of several oral and topical Janus kinase inhibitors, further studies are warranted.

Conflicts of interest

Angela Moore receives funds as an advisory board member (A), consultant (C), clinical study investigator (I), and speaker (SP) — for AbbVie (I,SP), Almirall (C,I,SP), Arcutis (I), Biofrontera (C,I), Boehringer Ingelheim (I),

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