

# Subacute thyroiditis in psoriasis patients treated with biologics targeting tumor necrosis factor- $\alpha$ and interleukin-17A, a report of two cases

Dear Editor,

Nowadays, biologics is an important therapeutic option for a variety of disease entities, including autoimmune, allergic, autoinflammatory, and inherited metabolic disorders.<sup>1</sup> Since most biologics are designed to act on specific components of immune system, they occasionally cause unexpected unusual side effects. Here we present two psoriasis patients treated with biologics who developed subacute thyroiditis (SAT), a rare subtype of thyroid gland inflammation, including the first case receiving anti-interleukin (IL)-17 therapy.

## Case 1

A 75-year-old man with a 27-year history of psoriatic arthritis consulted our hospital for episodic fever up to 38°C and sore throat. He had started bimonthly infliximab at the age of 66. Blood tests showed free T4, 0.37 ng/dL (reference range, 0.90-1.70); and thyroid-stimulating hormone (TSH), 12.79  $\mu$ IU/mL (reference range, 0.41-4.01). Ultrasound assessment of thyroid gland showed goiter with hypoechoic areas, which were consistent with the tenderness. With no medication, his symptoms improved, but hypothyroidism persisted for three months and required hormone replacement therapy.

## Case 2

A 78-year-old woman had a 12-year history of psoriasis. She started monthly secukinumab at the age of 77. Four months later, she complained of anterior neck discomfort, flu-like symptoms, and tenderness with swelling in thyroid gland. Blood tests showed C-reactive protein 19.0 mg/L (reference range, under 3.0); free T4, 1.73 ng/dL; and TSH, 0.49  $\mu$ IU/mL. Ultrasound assessment revealed characteristic findings of SAT including hypoechoic lesions with low vascularity in the affected areas. Oral prednisolone 20 mg/d rapidly resolved her symptoms.

Subacute thyroiditis is a self-limited thyroid disorder, which begins with a prodrome of generalized myalgias, pharyngitis, fever, and fatigue. Thyroid function test shows a triphasic course of hyperthyroidism, followed by hypothyroidism and ending with euthyroidism. Although viral causes have been proposed, clear evidence is lacking.<sup>2</sup> To date, four cases of SAT during anti-tumor necrosis factor (TNF) treatment for psoriasis were reported (Table 1).<sup>3-6</sup> Most authors inferred that TNF inhibitors induced an immunosuppressive status and rendered patients susceptible to viral infection. As for IL-17, recent studies indicate its involvement in thyroid disorders. Increased IL-17 production from T cells and Th17-skewed T cell induction were reported in Hashimoto's disease.<sup>7</sup> Likewise, serum IL-17 levels and IL-17 receptor A expression on thyrocytes were up-regulated in Graves' disease.<sup>8,9</sup> These observations imply that serum

**TABLE 1** Cases of psoriasis patients who developed SAT during biologics treatment

Biologics	Psoriasis type	Age/Gender/Race	Cause of SAT	Treatment for SAT	Number
Adalimumab	PsO	54/F/Caucasian	NK	Nonsteroidal anti-inflammatory drugs	Reference 3
Infliximab	PsA	47/M/Guadeloupean	Cytomegalovirus	None	Reference 4
Adalimumab	PsA	50/F/NK	NK	Corticosteroids	Reference 5
Adalimumab	PsA	41/F/Taiwanese	NK	Corticosteroids	Reference 6
Infliximab	PsA	75/M/Japanese	NK	None	Case 1
Secukinumab	PsO	78/F/Japanese	NK	Corticosteroids	Case 2

Abbreviations: F, female; M, male; NK, not known; PsA, psoriatic arthritis; PsO, plaque psoriasis; SAT, subacute thyroiditis.

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IL-17 level alteration can affect thyroid gland and might have driven inflammation in our case 2.

In contrast to anti-TNF therapeutics with a more than 20-year history, therapies targeting the IL-23/IL-17 pathway have just started, as is the case with secukinumab, a humanized IgG1 antibody binding to IL-17A, firstly approved in 2014. IL-17 is a cytokine whose function is not fully investigated. For instance, IL-17 has been demonstrated to be involved in inflammatory bowel disease, but secukinumab was proved to deteriorate Crohn's disease.<sup>10</sup> In the era of biologics, clinicians should be attentive to adverse events, so that we can accumulate safety profiles of a new therapy and may contribute to unraveling the molecular basis of unknown pathophysiology.


#### CONFLICT OF INTEREST

The authors have declared that no conflict of interest exists.

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