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Case Report

Ustekinumab successfully treated a patient with severe psoriasis vulgaris with primary failure to infliximab and secondary failure to adalimumab

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ABSTRACT

Biologic drugs have been recently used to treat psoriasis. However, some patients do not respond or lose therapeutic benefit with first-line use of tumor necrosis factor (TNF) antagonists. We report a case of psoriasis vulgaris, that failed to respond to TNF antagonists, infliximab and adalimumab, completely disappeared after treatment with ustekinumab, a therapeutic agent for biologically blocking p40 protein of interleukin (IL) 12 and 23. This report highlights anti-TNF agents only inhibited the TNF-α/inducible nitric oxide synthase (iNOS)-producing dendritic cells (TIP-DCs), but the plasmacytoid-DC-derived psoriatic response was re-initiated. On the other hand, ustekinumab may inhibit both the TIP-DCs and the plasmacytoid-DC-derived inflammatory response.

Key words: Ustekinumab; psoriasis; psoriasis vulgaris; infliximab; adalimumab

INTRODUCTION

Psoriasis is a common, chronic inflammatory skin disease [1,2]. Patients with psoriasis experience a significant reduction in quality of life and psychosocial disability; this emphasizes the need for prompt, effective treatment and long-term disease control [2]. Recently, psoriasis has been treated with biologic agents that selectively block specific steps in the inflammatory cascade [2]. For example, tumor necrosis factor (TNF) antagonists, including infliximab and adalimumab, have proven to be highly effective in treating psoriasis, because TNF-α plays a central role in the inflammation underlying psoriasis [3]. However, some patients do not respond or lose therapeutic benefit with anti-TNF antagonists [4]. Ustekinumab is a fully humanized monoclonal antibody that binds to the shared p40 subunit of interleukin (IL) 12 and 23. Ustekinumab was recently approved by the National Institute for Health and Clinical Excellence for first-line use or for treatment after failure with an anti-TNF antagonist [4]. Here, we describe a patient with severe psoriasis that was successfully treated with ustekinumab after responding poorly to two TNF antagonists, infliximab and adalimumab.

CASE REPORT

A 46-year-old female (weight, 51 kg) was referred to our department with refractory psoriasis that had lasted 7 years. Previous unsuccessful treatments included topical therapies, including topical corticosteroids and vitamin D3, and a systemic cyclosporine. Before TNF antagonist treatment, her assessment of the condition of psoriasis was as follows: psoriasis area and severity index (PASI): 11.2 (Fig. 1); physician's global assessment (PGA): 3; and Dermatology Life Quality Index (DLQI): 17. Clinical and laboratory investigations were performed to exclude active tuberculosis and possible systemic infections. The hepatitis B (HB) core antibody (HBcAb) test was positive, but HBV surface antigen, HBV e-antigen, and HBV DNA tests were negative. Aspartate aminotransferase and alanine aminotransferase levels were within normal

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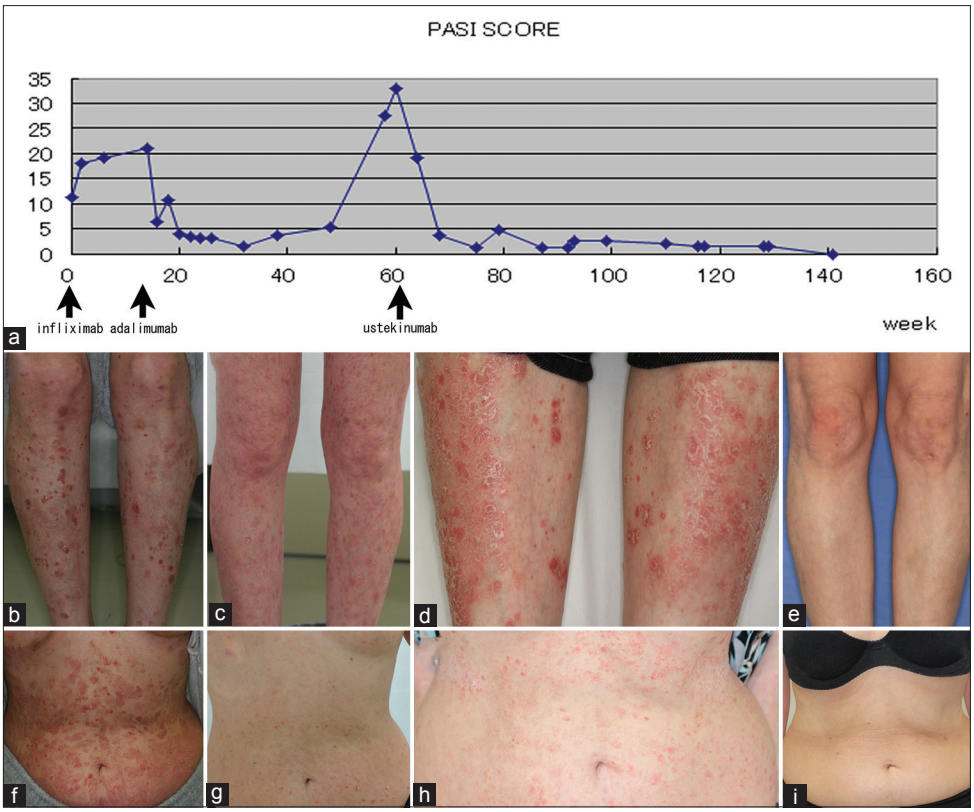

Figure 1: (a) Psoriasis Area and Severity Index (PASI) scores throughout the time course (b) (f) Psoriatic plaques on the lower extremities (b) and the abdomen (f) before infliximab (c) (g) Skin lesions on the lower extremities (c) and the abdomen (g) before adalimumab (d) (h) Flare-up of new plaques with severe scales on the lower extremities (d) and the abdomen (h) before ustekinumab (e) (i) Complete clearance of psoriasis on the lower extremities (e) and the abdomen (i) at 77 weeks after starting ustekinumab.

ranges. In March 2010, we administered intravenous infusions of infliximab (5 mg/kg) at 0, 2, and 6 weeks. At 14 weeks, she achieved a partial response, but exhibited PASI: 21, PGA: 4, and DLQI: 21 (Fig. 1). Therefore, we decided to withdraw infliximab therapy. In June 2010, we initiated subcutaneous adalimumab (40 mg) injections every 2 weeks. Twice, she received 80 mg of adalimumab, but then she declined 80 mg and reduced the amount to 40 mg due to its high cost. After 48 weeks, the psoriatic skin lesions worsened, with PASI: 33, PGA: 4, and DLQI: 24. In June 2011, we switched to ustekinumab because we considered secondary failure of adalimumab (Fig. 1). Ustekinumab (45 mg) was injected subcutaneously at 0 and 4 weeks. At week 4, the patient achieved a PASI 75. She continued ustekinumab treatment with injections every 12 weeks. She achieved PASI 90 and PGA: 0 after the third treatment. Her psoriasis remained well-controlled for 3.5 years. HBV DNA has remained negative.

DISCUSSION

Biologic agents that selectively block steps in the inflammatory cascade can control severe psoriasis. These agents have increased our understanding of the immunologic and pathophysiological basis of psoriasis. Psoriasis is driven and maintained by multiple components of the immune system. Although long been assumed to be a disorder in T helper type 1 (Th1) cells, recent evidence indicated that psoriasis pathophysiology also involves TNF-α, inducible nitric oxide synthase (iNOS)-producing dendritic cells (TIP-DCs), and Th17 cells. This was highlighted by the remarkable clinical efficiency of anti-TNF antagonist and anti-IL-12/23-p40 antibodies in treating psoriasis. Nevertheless, the TIP-DC-Th17 cell theory cannot explain the unique clinical finding, known as the paradoxical side-effect, where psoriasiform and pustular eruptions develop during anti-TNF therapy [5]. Therefore, it was proposed that plasmacytoid DCs were also involved in psoriasis pathophysiology [1]. Plasmacytoid DCs initiate psoriasis through production of interferon-α (IFN-α) [1]. TNF inhibits plasmacytoid DC generation and also inhibits IFN-α release by plasmacytoid DCs [1]. The TIP-DCs are inhibited by anti-TNF agents, but the plasmacytoid-DC-derived psoriatic response may be re-initiated [5]. The presented case demonstrated that ustekinumab could effectively treat severe psoriasis

that was unresponsive to anti-TNFα preparations. We hypothesized that anti-TNF agents only inhibited the TIP-DCs, but the plasmacytoid-DC-derived psoriatic response was re-initiated; thus, ustekinumab may inhibit both the TIP-DCs and the plasmacytoid-DC-derived inflammatory response. Further studies are needed to evaluate these treatments and to determine the role of ustekinumab in psoriasis management.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles.

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