

CASE REPORT

# A Case of Recalcitrant Psoriatic Arthritis to TNF Inhibitors Improved After Administration of Secukinumab, an IL-17A Inhibitor

Eleftherios Pelechas · Tereza Memi · Paraskevi V. Voulgari · Alexandros A. Drosos

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## ABSTRACT

Psoriatic arthritis (PsA) is a unique inflammatory arthritis due to the fact that patients have to deal not only with pain but also with their skin appearance, which may have a detrimental effect on their everyday lives and psychology. Treating a patient with PsA, improving both the musculoskeletal and skin symptoms is a challenge for the clinical rheumatologist. In this case, we present a patient of recalcitrant PsA to tumor necrosis factor inhibitors (TNFi) who had an exceptional improvement after administration of the interleukin-17A inhibitor (IL-17Ai) secukinumab.

**Keywords:** IL-17A inhibitor; Psoriatic arthritis; Secukinumab; TNF inhibitors

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E. Pelechas · T. Memi · P. V. Voulgari ·  
A. A. Drosos (✉)  
Rheumatology Clinic, Department of Internal  
Medicine, Medical School, University of Ioannina,  
Ioannina, Greece  
e-mail: adrosos@cc.uoi.gr

## INTRODUCTION

In the pre-TNF inhibitors (TNFi) era, there were enough cases of recalcitrant, moderate-to-severe, psoriatic arthritis (PsA) [1, 2]. Glucocorticoids (GCs), synthetic disease-modifying antirheumatic drugs (sDMARDs), retinoids, and photochemotherapy were the mainstay treatment for those cases, often with poor physician expectations because of significant side effects [3]. Since the approval of TNFi treatment for PsA, recalcitrant cases showed a dramatic decrease [4, 5]. The introduction of the TNFi in the early 2000s, the first biologic disease-modifying antirheumatic drugs (bDMARDs) used in the treatment of PsA, showed a significant capacity to achieve states of low disease activity or remission and became the gold standard treatment with a promising efficacy/safety profile [6, 7]. The first TNFi for moderate-to-severe PsA was etanercept [8]. Nowadays, the clinician has an extended armamentarium to combat PsA with new biologic agents already available (Table 1) or still under research.

We present a case of recalcitrant PsA to two TNFi, which showed a remarkable improvement after administration of secukinumab, an IL-17A inhibitor.

Informed consent, for the publication for this case report and any additional related information was taken from the patient involved in the study.

**Table 1** Biologic agents for PsA

Treatment	Target	Year of approval
Etanercept	TNFi	2002
Adalimumab	TNFi	2005
Infliximab	TNFi	2005
Golimumab	TNFi	2009
Certolizumab Pegol	TNFi	2013
Ustekinumab	IL12/IL23	2013
Apremilast	PDE4	2014
Secukinumab	IL17A	2016
Inflectra	TNFi–Biosimilar	2015

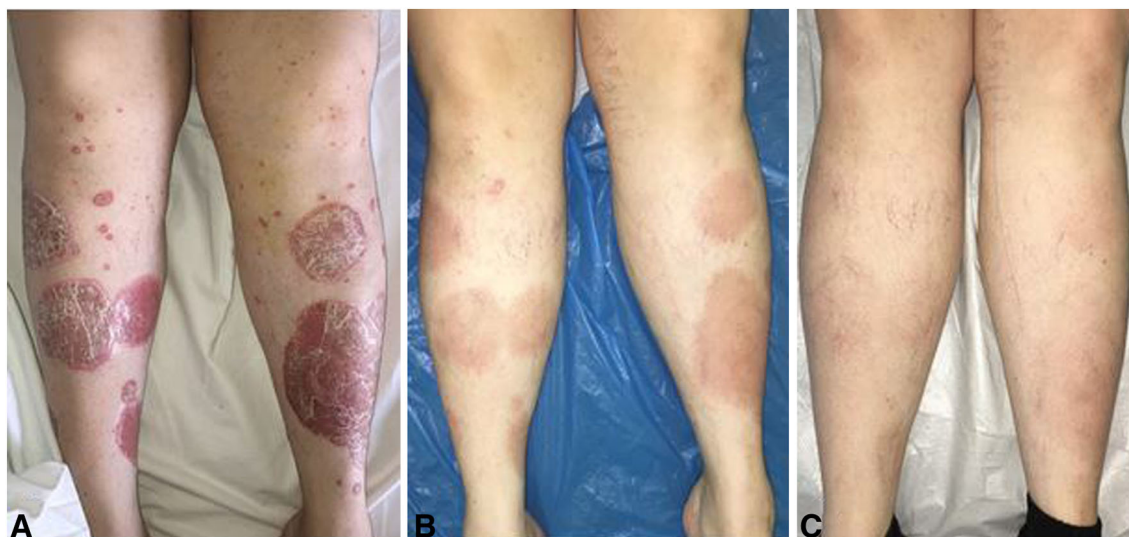
## CASE REPORT

A 37-year-old female presented to our outpatient rheumatology clinic because of severe plaque psoriasis and arthritis involving the large joints, mainly knees, left ankle, and left elbow. She had been diagnosed with psoriasis since the age of 13, and she had been treated with topical therapy with some improvement. She had no arthritis at that time and she developed asymmetrical polyarthritis 2 months prior to her visit to our department. Past medical and family history were unremarkable, and after an appropriate screen test, she was treated with methotrexate (MTX/15 mg/week) and small doses of prednisone (7.5 mg/day). After 2 months, she showed some clinical improvement, but her liver enzymes were elevated (AST 127 IU/L, ALT 120 IU/L), thus MTX was discontinued and cyclosporine-A (CSA/200 mg/day) was added. After 3 months of CSA therapy she showed clinical improvement of skin manifestations but synovitis of both knees was evident with high acute phase reactants. Adalimumab was added (40 mg/14 days) subcutaneously with significant clinical and laboratory improvement. However, after 8 months of adalimumab and CSA treatment, she had a disease flare-up with symmetrical synovitis, including both knees and ankles, as well as severe skin manifestations. Both drugs were

discontinued and etanercept (50 mg/week) subcutaneously and leflunomide (20 mg/day) were started. Three months later, she had a significant clinical and laboratory response but she developed elevated liver enzymes once again. A workup for liver disease (ultrasonography, screening for hepatitis B and C) was negative. Leflunomide was discontinued and she carried on with etanercept (50 mg/week). She did quite well, but after 7 months of etanercept treatment she developed severe exacerbation of both skin and musculoskeletal involvement with disease activity score (DAS 28) 5.2 and a Psoriasis Area Severity Index (PASI) score 10.8 (Fig. 1a). After discussion with the patient, there was a switch from TNFi to secukinumab, an IL-17a inhibitor. She started on 300 mg s.c. on weeks 0, 1, 2, and 4 and monthly thereafter. On week 4, the patient came for follow-up and re-evaluation (Fig. 1b). She reported that except for the rapid skin improvement, there was a significant musculoskeletal improvement that she had never experienced in the past while using different sDMARDs or TNFi. PASI score was 2 and DAS 28 was 2.3. Secukinumab showed a dramatic and rapid response in the reduction of pain, followed by improvement of laboratory and clinical signs of joint inflammation. Skin disease also responded well after a short period of time which had a positive impact on patients' psychology. After 36 weeks of treatment with secukinumab, she is now free of joint pain and her skin has a near-normal appearance (Fig. 1c).

## DISCUSSION

Treating a patient with PsA and improving both the musculoskeletal and skin symptoms is a challenge for the clinical rheumatologist. PsA is a unique inflammatory arthritis due to the fact that these patients have to deal not only with pain but also with their skin appearance, which may have a detrimental effect on their everyday live and psychology [9]. Many authors correlate PsA with anxiety and depression [9, 10], which may lead to flare-ups of the disease, and in fact there is a vicious circle between disease activity and psychological status of the patient.



**Fig. 1** a Skin involvement while on etanercept. b Marked improvement on week 4 of secukinumab administration. c Significant improvement on week 36 of secukinumab administration

As mentioned above, the number of patients with recalcitrant PsA has declined since the introduction of TNFi. Nevertheless, there are cases, like the one we present in the current report, that show a particular resistance to TNFi. Current guidelines propose the use of a second TNFi when the first TNFi fails to prove success regarding disease activity. Secukinumab is a new, promising biologic agent with rapid results and a good safety profile [11]. This is the first case the authors are aware of in Greece since the approval of secukinumab in January 2016 for the treatment of moderate-to-severe PsA showing significant improvement of synovitis and plaque psoriasis after failing in two TNFi and three sDMARDs. An interesting article from Kurosaki et al. describes a case of refractory psoriasis and pruritus, which became unresponsive to several biologics (ustekinumab, adalimumab, infliximab plus MTX). Treatment was switched to secukinumab, and after 32 weeks, PASI 100 was achieved [12].

Data from the clinical literature on switching bDMARD therapies in PsA are limited. In general, numerous bDMARDs have demonstrated efficacy in PsA, including the TNFi, the IL-12/23 inhibitor ustekinumab, and the IL-17A inhibitor secukinumab, but there are limited data on cases of recalcitrant PsA. The IL-17A

inhibitor secukinumab is approved for the treatment of moderate-to-severe plaque psoriasis, ankylosing spondylitis, and PsA. Results of large-scale phase 3 studies indicate that secukinumab significantly improves the signs and symptoms of PsA in both TNFi-naïve and TNFi-experienced patients.

Mease et al. [13], in a phase 3 study (FUTURE 1), reported that among patients who had a previous inadequate response to TNFi therapy or who had unacceptable side effects, an American College of Rheumatology 20% improvement criteria (ACR20) response was reported in 23 of 59 patients (39%) who received 150 mg of secukinumab, 23 of 60 patients (38.3%) who received 75 mg of secukinumab, and ten of 59 patients (16.9%) in the placebo group. In a post hoc analysis, ACR20 response rates were better in the secukinumab groups than in the placebo group at week 24, regardless of concomitant MTX use.

McInnes et al. [14], in a randomized, double-blind, placebo-controlled, phase 3 trial (FUTURE 2), showed that in prespecified exploratory analyses, ACR and PASI response rates were higher with secukinumab than with placebo in both TNFi-naïve and TNFi-experienced patients with the magnitude of response generally being higher in the TNFi-naïve population (Table 2).

**Table 2** Efficacy of secukinumab at week 24 in TNFi-naive and TNFi-experienced patients

	ACR20 (%) <sup>a</sup>	ACR70 (%)	PASI75 <sup>b</sup> (%)	PASI90 (%)
Secukinumab				
300 mg				
TNFi-n	58	22	63	53
TNFi-e	45	15	64	36
Secukinumab				
150 mg				
TNFi-n	63	27	56	39
TNFi-e	30	11	36	23
Secukinumab				
75 mg				
TNFi-n	37	6	30	12
TNFi-e	15	6	24	12
Placebo group				
TNFi-n	16	2	19	10
TNFi-e	14	0	8	8

<sup>a</sup> American College of Rheumatology 20% improvement criteria

<sup>b</sup> Psoriasis Area and Severity Index

## CONCLUSIONS

In conclusion, secukinumab seems to be a reasonable choice in cases of recalcitrant PsA patients to other biologic treatments due to the fact that IL-17A is an important factor involved in the pathogenesis of psoriatic lesions. In addition, downregulation of proinflammatory cytokines such as IL-1, IL-6, and TNF $\alpha$ , possibly augment the therapeutic potency of secukinumab [15].

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**Disclosures.** Eleftherios Pelechas, Tereza Memi, Paraskevi V. Voulgari and Alexandros A. Drosos have nothing to disclose.

**Compliance with Ethics Guidelines.** Informed consent for the publication for this case report and any additional related information was taken from the patient involved in the study.

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