

Case and Review

Optimizing Secukinumab Treatment in Psoriasis with Concomitant Methotrexate Administration: Minireview and A Case Report

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Keywords

Psoriasis · Psoriatic arthritis · Secukinumab · Methotrexate concomitant therapy

Abstract

The introduction of biologic drugs for the treatment of moderate-to-severe psoriasis resulted in a significant improvement in patients' health. Moreover, treatment regimens in psoriatic patients should be tailored to meet specific needs based on disease severity, impact on quality of life, response to previous therapies and presence of comorbidities. Combination therapy of biologic agents with conventional systemic drugs has been proposed to optimize psoriasis treatment outcomes in unresponsive or partial responsive severe psoriatic patients. We report the case of a patient with a long-standing recalcitrant plaque psoriasis and psoriatic arthritis who was administered secukinumab combined with methotrexate. The patient had previously been treated with several topical and systemic therapies associated with loss of efficacy or adverse event occurrence. Approximately 24 weeks after starting the combined regimen, significant clearance of psoriasis and reduction of arthritis ensued, with no drug side effects.

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Combination Therapy of Biologic Agents with Conventional Systemic Drugs in Psoriasis

The introduction of biologic drugs for the treatment of moderate-to-severe psoriasis resulted in a significant improvement in patients' health. For years, PASI75 has been the gold standard endpoint, but today PASI90 and PASI100 are being used more extensively, as therapies have become more efficient and patient expectations toward treatments have increased [1]. Thanks to improved availability, treatment regimens for psoriatic patients should be tailored to meet specific needs based on disease severity, impact on quality of life, response to previous therapies and presence of comorbidities. Several strategies are being used to manage unresponsive patients who experience a loss of efficacy after an initial clinical response to systemic therapy. Combination therapy of biologic agents with conventional systemic drugs has been proposed to optimize psoriasis treatment outcomes [2]. The benefit of the combination therapy is the ability to overcome individual drug limitations, including lack of efficacy or efficacy reduction due to the prolonged use or due to the natural fluctuations in disease activity, typical in psoriasis, and adverse events. Moreover, drugs with different mechanisms of action provide an additive or synergistic effect, reducing the required doses of each single agent, limiting the side effects. Concomitant administration of methotrexate with biologics may prevent or diminish the antidrug antibodies development, improving response rates [3]. Furthermore, the dose of methotrexate can be reduced when a biologic drug is added, with a decrease in the risk of end-organ toxicity in cardiopathic patients or in the risk of fatty liver and hepatic fibrosis in obese patients, both associated with long-term use of drugs [4, 5]. Although it has not been extensively investigated in psoriasis, the combination therapy seems to be used quite often in clinical practice. According to the literature, up to 30% of psoriatic patients on tumour necrosis factor- α inhibitors concomitantly receive therapy with a conventional systemic agent such as methotrexate [6, 7]. When used in combination, methotrexate not only exerts its independent clinical effect but also works synergistically to improve clinical efficacy of tumour necrosis factor- α inhibitors [8].

Secukinumab in Psoriasis and Psoriatic Arthritis

Secukinumab is an interleukin-17A inhibitor that has shown significant efficacy in the treatment of moderate-to-severe psoriasis and psoriatic arthritis (PsA), demonstrating a rapid onset of action, sustained response, a favourable safety profile, and an improvement of patients' quality of life [9]. Although secukinumab has shown good results both in clinical trials and in a real-life setting, clinicians may need to optimize its administration in problematic patients. In clinical trials, secukinumab was added to methotrexate, in patients with PsA and ankylosing spondylitis [10]. Combination therapy of secukinumab with methotrexate has been reported in 2 patients [11], while secukinumab/apremilast administration was described in a case report [6]. Significant clinical improvement and minimal drug side effects were confirmed in these patients. On the other hand, the mechanisms underlying the effects of secukinumab/methotrexate combination have not been investigated. In particular, the role of methotrexate in immunogenicity inhibition seems not to be relevant, as secukinumab per se was demonstrated to have a very low potential in inducing antidrug antibodies, if compared to other biologics currently used in psoriasis treatment [12, 13].

Case Report

We report a 70-year-old Caucasian woman with a long-standing, moderate-to-severe, recalcitrant plaque psoriasis and PsA, who achieved near-complete clinical clearance on a combination of secukinumab and methotrexate. The patient developed plaque type psoriasis at the age of 50, while symptoms of symmetric peripheral polyarthritis, seronegative for rheumatoid factor, occurred approximately 8 years later. For several years, her disease was poorly managed. More recently, she received appropriate topical therapy (e.g., tar, corticosteroids, and vitamin D analogues) but remained refractory to treatment, requiring systemic therapy. She was initially treated with 15 mg per week of oral methotrexate, resulting in excellent improvement, which unfortunately led to significant abnormal findings on her liver functions, leading to methotrexate discontinuation. Then, several biological treatments, including etanercept, adalimumab, and ustekinumab, were used at recommended doses and discontinued due to relapse of skin disease or worsening of articular symptoms, after a median of 9 months of therapy. As skin psoriasis and joint symptoms were worsening, treatment with secukinumab was initiated at the end of September 2017. At the time of secukinumab introduction, the patient had diffuse erythematous, inflammatory patches and plaques covered with white scales, involving 45% of the body surface area (BSA) and a Psoriasis Area and Severity Index (PASI) score of 26 (Fig. 1). The patient received 5 subcutaneous secukinumab (300 mg weekly) injections, followed by once-a-month injections. After 4 weeks of treatment, the patient showed a rapid improvement with a reduction of the PASI score to 11 and of BSA involvement to 23%. Nevertheless, in February 2018, the patient experienced a rapid worsening of her psoriasis with BSA involvement of 60% and PASI score of 31.8. Clinical examination showed an increase in erythema and scaling; superficial exfoliation of the trunk and buttocks were noted (Fig. 2). Therefore, we decided to add methotrexate 10 mg s.c. per week. A low dosage was administered because of the previously depicted occurrence of adverse events. After 24 weeks of combination therapy, the disease was stabilized, with mild erythema involving 1% of BSA, a PASI score of 1.2, and a satisfactory control of joint symptoms, without side effects (Fig. 3).

Discussion

Combination systemic drug therapy may be an effective and tolerated option for the management and treatment of severe psoriasis patients. In the case report described, after repeated therapy failures, treatment was optimized by adding methotrexate to secukinumab. Concomitant administration of a biologic drug with low dosages of single traditional drugs may be used to obtain a clinical response with a reduced risk of adverse events.

Conclusion

Secukinumab has a favourable safety profile that makes it a good candidate for the concomitant use with traditional systemic drugs, lowering the adverse event risk.

Key Message

Combination therapy with secukinumab and methotrexate provides significant improvement in psoriasis and PsA, with no drug side effects.

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and accompanying images. The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors have been personally and actively involved in substantive work leading to the manuscript.

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Fig. 1. Clinical appearance before therapy with secukinumab.



Fig. 2. Clinical worsening 20 weeks after secukinumab monotherapy.

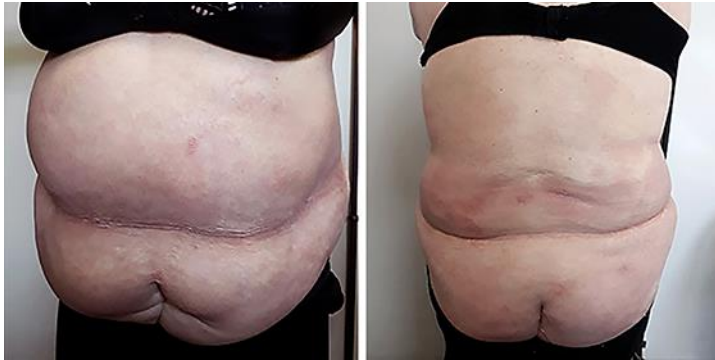


Fig. 3. Significant clinical improvement 24 weeks after combination therapy with secukinumab and methotrexate.