Dual Improvements in Dermatological Symptoms and Psychological Well-Being of Psoriasis Patients After Treatment with a Single Dose of Secukinumab: Three Case Reports

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ABSTRACT:
Psoriasis is a chronic inflammatory skin condition that significantly impacts the physical and psychological well-being of affected individuals. It is characterized by well-demarcated, erythematous plaques with a white scaly surface. Beyond its dermatological manifestations, psoriasis is associated with systemic comorbidities, including arthritis, metabolic syndrome, cardiovascular diseases, and notably, psychological disorders such as depression and anxiety. We report a case series of patients suffering from moderate to severe psoriasis with concurrent mild to moderate depression. Patients administered with a single dose of 300 mg secukinumab, an interleukin-17 antagonist, showed significant improvements in psoriasis symptoms, quality of life, and depression levels within an 8-week period. This dual benefit underscores the importance of an integrated approach to managing patients with psoriasis, addressing both dermatological and psychological aspects.
Key words: Psoriasis**,** Secukinumab, Interleukin-17 antagonist, Psychological well-being, Depression, Quality of life

Introduction

Psoriasis is a common chronic inflammatory skin disease influenced by the immune system[1], impacting around 2% of the global population[2]. Numerous clinical subtypes exist, with the most common manifestation being plaque-type psoriasis. This is recognized by well-demarcated, erythematous plaque with a white scaly surface, typically found on extensor surfaces of the extremities, hands, feet, scalp, and the lower back. Patients are experiencing sensations of stinging, pruritus, and discomfort[3].

Psoriasis is correlated with other systems, encompassing arthritic, metabolic, cardiovascular, and psychological comorbidities. The etiology of psoriasis is multifactorial composed of genetic predisposition, immunological elements, and environmental triggers, notably psychological stress, which is a pivotal factor in precipitating disease exacerbation[4].

We report a case series of patients diagnosed with moderate to severe psoriasis accompanied by mild to moderate depression. Following the administration of a single dose of an IL-17 antagonist, the improvements in both psoriasis symptoms, quality of life, and depression levels were observed.

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Case report

Patient I

A 65-year-old Thai female has been diagnosed with psoriasis vulgaris and psoriatic arthritis for 9 years. Her current medication regimen consists of methotrexate at a dosage of 12.5 milligrams per week (with a cumulative dose of 1,965 milligrams), combined with topical steroid and topical calcipotriol. However, there has been no improvement in her skin lesions. Upon dermatological examination, multiple well-defined erythematous plaques with silvery scales were observed, affecting 40% of the body surface area, including the scalp, trunk, and extremities (Figure 1A).

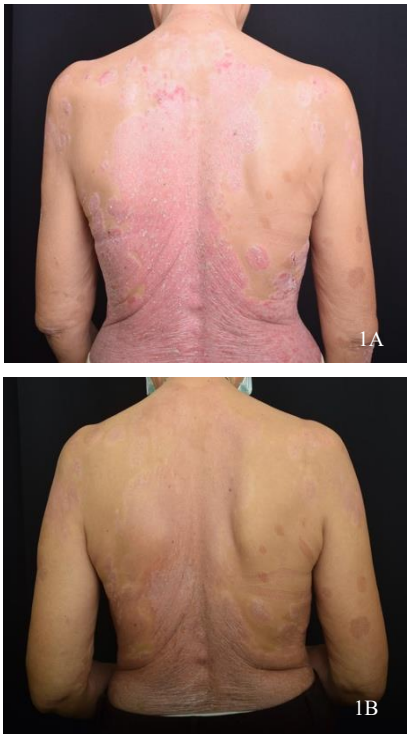

Figure 1 Clinical manifestations of Patient I: (A) before and (B) after 8 weeks of treatment with a single dose of secukinumab

The assessment tools utilized included the Psoriasis Area and Severity Index (PASI) and the 6-point scale Physician Global Assessment (PGA) for assessing disease activity; the Dermatology Life Quality Index (DLQI)[5] and the EuroQol-5 Dimension (EQ-5D)[6] for evaluating health-related quality of life; and the Patient Health Questionnaire (PHQ-9)[7] for depression. The baseline PASI score was 22.4, with a PGA score of 5, indicating severe psoriasis lesions. The DLQI score was 9, reflecting a moderate impact of psoriasis on the patient's quality of life. The EQ-5D utility score was 0.76, indicating the impact of psoriasis on health-related quality of life from the patient's perspective. Additionally, the Patient Health Questionnaire (PHQ-9) score was 11, suggesting moderate depression (Figure 4A-E).

Treatment options were discussed with the patient, and it was decided to initiate treatment with secukinumab, an IL-17 antagonist, at a dosage of 300 milligrams subcutaneously. Due to financial constraints and limitations in accessing biologic therapy, the patient received a single dose of secukinumab, in combination with methotrexate, topical steroid, and topical calcipotriol. The patient's disease activity, quality of life, and depression were assessed at 2 weeks, 4 weeks, and 8 weeks post-administration of secukinumab, utilizing PASI, PGA, DLQI, EQ-5D, and PHQ-9 scores (Figure 4A-E).

Two weeks post-administration: a significant improvement in skin lesions was noted, with the PASI score decreasing to 11.7 and the PGA score improving to 3. The patient’s depression and quality of life also showed marked improvement, as demonstrated by a reduction in the PHQ-9

score to 5 (mild depression), a decrease in the DLQI score to 7, and an increase in the EQ-5D score to 0.93.

Four weeks post-administration: the PASI score further reduced to 10, while the PGA score remained stable at 3. The patient's quality of life and depression scores stayed consistent with the 2-week mark, with the DLQI and EQ-5D scores unchanged at 7 and 0.93, respectively, and the PHQ-9 score remaining at 5.

Eight weeks post-administration: there was continued improvement in the patient's skin condition (Figure 1B), with the PASI score further decreasing to 8.3 and the PGA score improving to 2. Notably, there was a significant enhancement in the quality of life, evidenced by a DLQI score reduction to 4 and an EQ-5D score improvement to 1. Additionally, depressive symptoms further decreased, with the PHQ-9 score lowering to 4, indicating mild depression.

Patient II

A 36-year-old Thai male has been diagnosed with psoriasis vulgaris for 5 years. He also has underlying type 2 diabetes mellitus, hypertension, and dyslipidemia. His treatment regimen has included methotrexate at a dosage of 10 milligrams per week (with a cumulative dose of 260 milligrams), combined with phototherapy (narrow band UVB) twice weekly, and topical steroid application for psoriasis management. Upon dermatological examination, multiple well-defined erythematous plaques covered with silvery scales were observed, affecting 40% of the body surface area, including the scalp, trunk, and extremities (Figure 2A).

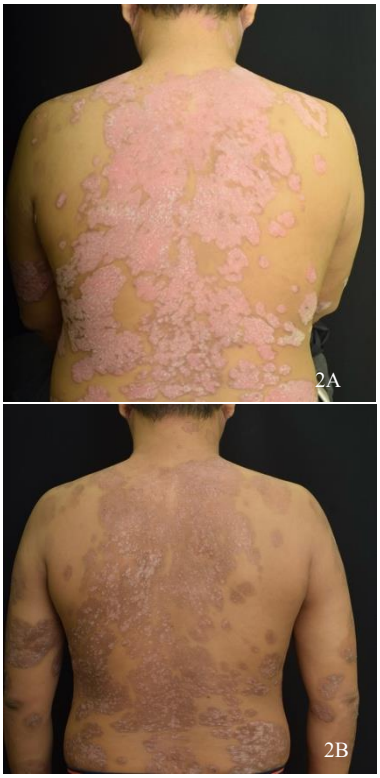

Figure 2 Clinical manifestations of Patient II: (A) before and (B) after 8 weeks of treatment with a single dose of secukinumab

Baseline assessments revealed a PASI score of 19.8 and a PGA score of 6, highlighting the significant impact of the disease on the patient's quality of life, as indicated by the DLQI and EQ-5D scores of 13 and 0.7, respectively. Additionally, mild depression was noted, with a baseline PHQ-9 score of 7 (Figure 4A-E).

After a thorough discussion of treatment options, it was decided to initiate therapy with secukinumab, an IL-17 antagonist, administered subcutaneously at a dosage of 300 milligrams as a single dose, owing to financial constraints and limitations in accessing biologic therapy through the

healthcare scheme. This treatment approach was combined with methotrexate at a dosage of 10 milligrams per week, phototherapy (narrow band UVB) twice weekly, and topical steroid application.

Evaluations of the patient's psoriasis disease activity, quality of life, and depression were conducted at 2-, 4-, and 8-weeks post-administration of secukinumab, utilizing PASI, PGA, DLQI, EQ-5D, and PHQ-9 scores (Figure 4A-E).

Two weeks post-administration: the initial response to treatment was promising, with a decrease in the PASI score to 13.4 and the PGA score to 4, indicating a reduction in the severity of psoriasis. Additionally, there was an improvement in the patient's quality of life and mental health, as evidenced by the DLQI score decreasing to 10, the EQ-5D score increasing to 0.8, and the PHQ-9 score reducing to 5.

Four weeks post-administration: the patient's condition continued to improve, with a further reduction in the PASI score to 9.9. The PGA score remained stable at 4. The DLQI and EQ-5D scores remained stable at 9 and 0.8, respectively, indicating maintenance of the initial quality of life improvement. The PHQ-9 score also remained stable at 5.

Eight weeks post-administration: the patient showed continued improvement in psoriasis symptoms (Figure 2B), with the PASI score decreasing further to 8.3. The PGA score remained stable at 4. Notably, the quality of life showed additional improvement, with the DLQI score decreasing to 7 and the EQ-5D score increasing to 0.93. Furthermore, the PHQ-9 score decreased to 3, signaling a further reduction in depressive symptoms.

Patient III

A 25-year-old Thai female, diagnosed with psoriasis vulgaris for 6 years and without any underlying diseases, had previously undergone alternative medicine treatment for 1 year. Three months prior to her hospital visit, she experienced generalized erythema of the skin accompanied by desquamation. Dermatological examination revealed generalized erythroderma characterized by skin desquamation, along with multiple well-defined erythematous plaques covered with thick silvery scales, affecting over 90% of the body surface area (Figure 3A).

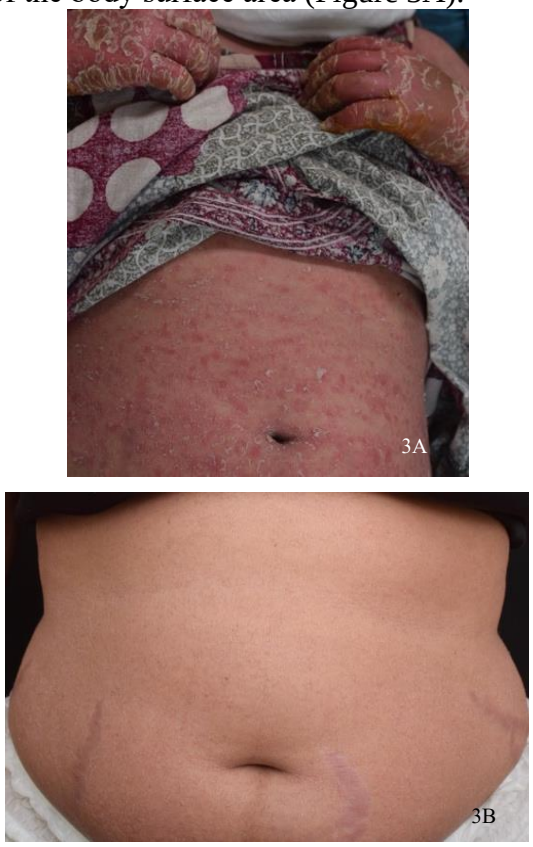

Figure 3 Clinical manifestations of Patient III: (A) before and (B) after 8 weeks of treatment with a single dose of secukinumab

Initially, the patient's PASI and PGA scores were 49.9 and 6, respectively, delineating a severe psoriatic involvement that extensively impaired her quality of life and significantly restricted daily functionalities. The DLQI and EQ-5D scores were 27 and 0, respectively, highlighting substantial impacts on her well-being. Concurrently, moderate depressive symptoms were quantified with a PHQ-9 score of 13 (Figure 4A-E).

Following a comprehensive discussion of treatment options with the patient and her family, therapy was initiated with secukinumab, administered subcutaneously at a dose of 300 milligrams. However, due to constraints within the healthcare scheme regarding access to biologic therapy and financial limitations, the patient was administered only a single dose of secukinumab. Subsequent evaluations of the patient's psoriatic disease activity, quality of life, and depression at 2-, 4-, and 8-weeks post-administration of secukinumab, utilizing PASI, PGA, DLQI, EQ-5D, and PHQ-9 scores, demonstrated considerable improvement (Figure 4A-E).

Two weeks post-administration: a notable decrement was observed in the PASI score to 28 and the PGA score to 5. The DLQI score persisted at 27, whereas the EQ-5D score was enhanced to 0.2. The PHQ-9 score remained unchanged at 13.

Four weeks post-administration: subsequent evaluations evidenced further clinical amelioration, with the PASI score reducing to 18.3 and the PGA score amending to 3. There was a notable decline in the DLQI score to 18, an increase in the EQ-5D score to 0.5, and a decrement in the PHQ-9 score to 7, highlighting an improvement in depressive symptoms.

Eight weeks post-administration: the patient demonstrated sustained improvement (Figure 3B), with the PASI score refined to 14.4 and the PGA score to 2. The DLQI score improved significantly to 10, and the EQ-5D score increased to 0.76. The PHQ-9 score was reduced to 4, indicating a resolution of depressive symptoms, thereby substantiating improvement in the severity of psoriasis, quality of life, and mental health status.

Discussion

Psoriasis is recognized as a chronic, relapsing condition that significantly impairs the quality of life and mental health of affected individuals. Particularly, early onset psoriasis is linked with psychological disturbances, including anxiety, depression, and suicidal ideation[4,8]. The psychological difficulties encountered by individuals with psoriasis arise from social stigmatization, workplace discrimination, and diminished self-esteem, which in turn are caused by the visibility of psoriatic lesions[8,9]. Stigmatization is particularly identified as a significant factor adversely affecting quality of life[10]. Additionally, higher scores on the PASI, body surface area, and DLQI correlate with greater instances of depression and anxiety[4,8,11]. This suggests that flares of psoriasis, induced by stress and depression, may contribute to a self-sustaining cycle of heightened stress and psychological distress[9].

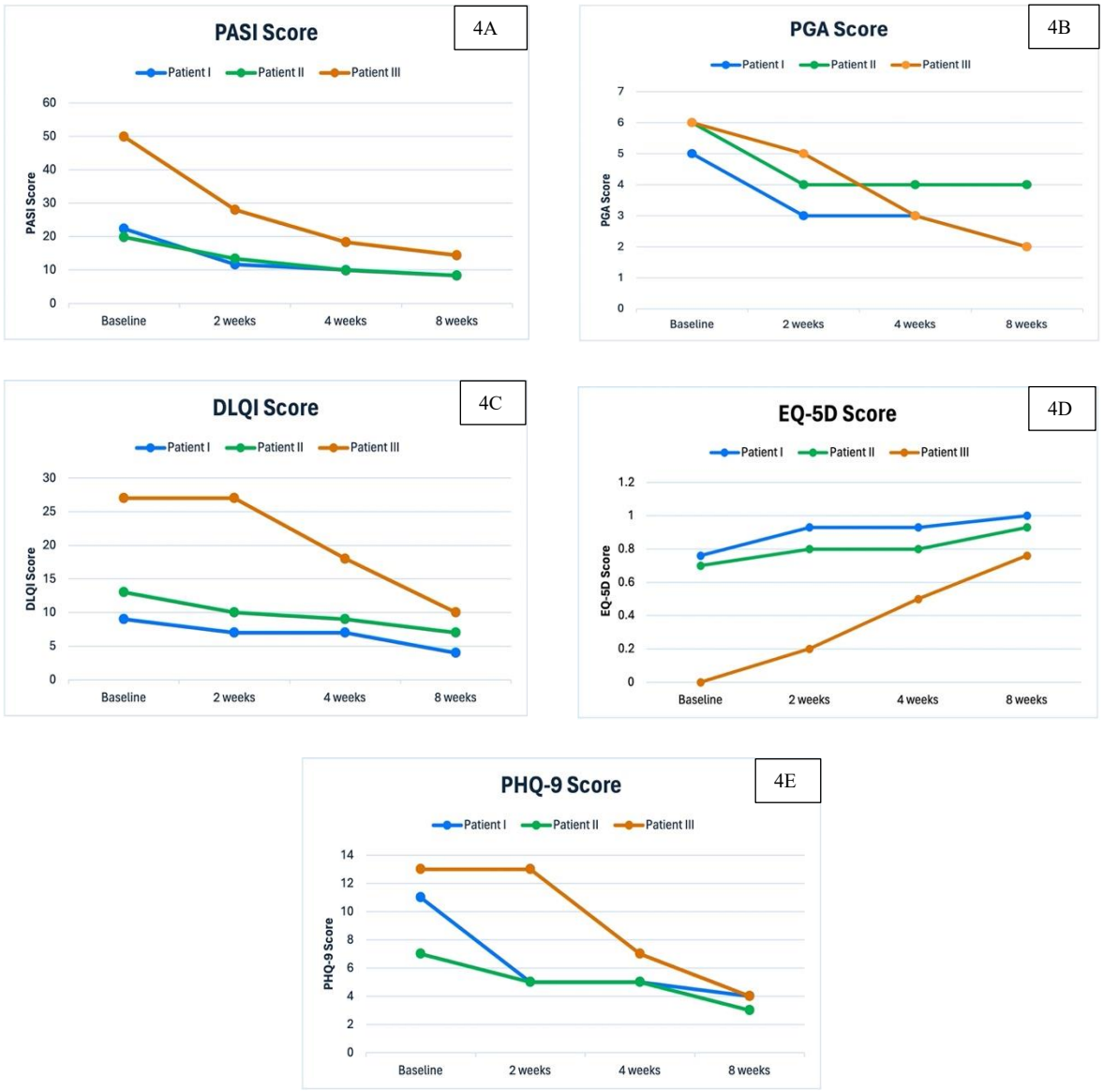

Figure 4 (A-E) The patient's PASI, PGA, DLQI, EQ-5D, and PHQ-9 scores at baseline, 2 weeks, 4 weeks, and 8 weeks post-administration of a single dose of secukinumab.

The pathogenesis of psoriasis involves a complex interplay of immune responses, characterized by the increased activation of T cells, macrophages, and dendritic cells. This immune response leads to an elevated release of proinflammatory cytokines, such as interleukin (IL)-6, IL-12, and tumor necrosis factor-alpha (TNF-α). Concurrently, the activation of Th17 cells by IL-23 triggers the release of IL-17 and IL-22, resulting in the proliferation of keratinocytes[12]. Notably, these proinflammatory cytokines implicated in psoriasis are also associated with

depression. For instance, the activation of the hypothalamic-pituitary-adrenal (HPA) axis by TNF-α, leading to tryptophan depletion and a subsequent decrease in serotonin levels, has been linked to the development of depression. Furthermore, elevated serum levels of TNF-α, IL-6, IL-17, and IL-23 have been observed in patients with depression[8].

Recent studies highlight the therapeutic potential of biologic agents in addressing both psoriasis and its psychological comorbidities. Timis, et al., documented a significant reduction in PHQ-9, GAD-7, PASI, and DLQI scores following a 6-month regimen of biologic therapy, including agents such as ixekizumab, secukinumab, guselkumab, certolizumab, ustekinumab, risankizumab, or adalimumab. This improvement in PASI scores correlated with a notable reduction in depression and anxiety severity[9]. Similarly, Talamonti, et al., reported that 48 months of secukinumab treatment for moderate to severe plaque psoriasis resulted in skin clearance and simultaneous improvements in anxiety, depression, and overall quality of life[13].

We present a case series of patients diagnosed with moderate to severe psoriasis, accompanied by mild to moderate depression, who initiated therapy with secukinumab, an IL-17 antagonist, administered subcutaneously in a single dose of 300 milligrams. After 2 weeks of treatment, patients showed improvement in PASI, PGA, DLQI, EQ-5D, and PHQ-9 scores. This improvement continued at 4- and 8-weeks post-administration of a single dose of secukinumab, with the maximum degree of improvement observed in the 8-week post-treatment. It is worth noting that since we assessed all scores only up to 8 weeks post-treatment, the improvement following a single dose of secukinumab represents an 8-weeks follow-up period. These findings, which correlate with those of the previously mentioned study, suggest that the alleviation of psoriatic symptoms may reduce social stigmatization and improve both the quality of life and mental health outcomes, including depression symptoms. Given the pathogenesis of psoriasis and depression, which involves an increase in proinflammatory cytokines including IL-17, further investigation is needed to determine whether skin clearance alone accounts for the improvement in depression or if the specific action of the IL-17 antagonist plays an additional role.

In conclusion, treatment with secukinumab, an IL-17 antagonist, in patients with moderate to severe psoriasis improves not only the severity of psoriasis but also the degree of depression, alongside an enhanced quality of life. Recognizing that patients with psoriasis are susceptible to psychological problems, the early detection and provision of long-term psychological support are crucial. This approach is imperative as psychological stress can trigger mental health issues, including depression and suicidal ideation, in these individuals.

Conflict of interest and funding

The authors obtained secukinumab samples from Novartis (Thailand) Limited for use in this case series due to the patients's inability to access biologic therapy through their healthcare scheme and financial constraints.

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