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USTEKINUMAB: A GENETICALLY ENGINEERED BIOLOGIC FOR PSORIASIS TREATMENT – A CASE REPORT

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Abstract

Introduction: One of the critical challenges in modern dermatology is ensuring the effectiveness of treatment for patients with moderate-to-severe psoriasis. The introduction of genetically engineered biological therapies targeting specific pro-inflammatory cytokines has significantly advanced the management of this condition and improved patients' quality of life.

The **aim** of the study is to evaluate the clinical effectiveness of ustekinumab in a patient with severe psoriasis.

Materials and Methods: A retrospective case analysis was conducted using the medical records of a single patient who received inpatient treatment at the dermatovenereology department of City Hospital № 2, under the Abay Regional Health Authority. The patient's condition was monitored through the Comprehensive Medical Information System (CMIS) during the period from 2011 to 2024. Diagnostic and therapeutic procedures were performed in accordance with the approved clinical protocol of the Ministry of Health of the Republic of Kazakhstan № 172, dated October 14, 2022. The publication of treatment outcomes was authorized by the hospital administration and the patient through signed informed consent.

Results: After the addition of Stelara to standard anti-inflammatory therapy, the patient's condition improved significantly. The drug alleviated symptoms such as skin itching, rashes, and joint pain. Clinical studies have demonstrated that ustekinumab effectively controls disease progression and enhances patients' quality of life by reducing pro-inflammatory cytokines and modulating anti-inflammatory markers. Research has also confirmed its efficacy in treating psoriatic arthritis symptoms and its success across diverse populations, with 67.2% of patients achieving PASI75 after two doses.

Conclusion: This clinical case demonstrates the effectiveness of ustekinumab in treating moderate-to-severe psoriasis complicated by psoriatic arthritis. The improvement in skin lesions, joint symptoms, and overall patient condition highlights the potential of biological therapy in disease management and enhancing quality of life.

Keywords: *psoriasis, ustekinumab, biological active drugs, case report.*

Резюме

УСТЕКИНУМАБ: ГЕННО–ИНЖЕНЕРНЫЙ БИОЛОГИЧЕСКИЙ ПРЕПАРАТ ДЛЯ ЛЕЧЕНИЯ ПСОРИАЗА – КЛИНИЧЕСКИЙ СЛУЧАЙ

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Введение: Одной из важных проблем в современной дерматовенерологии является проблема эффективности лечения больных псориазом со среднетяжелым и тяжелым течением. Внедрение генно-инженерной биологической терапии, направленной на таргетное воздействие путем блокирования конкретного провоспалительного цитокина позволило значительно продвинуться в вопросах терапии заболевания, а также улучшить качество жизни пациентов.

Цель исследования: оценка клинической эффективности препарата Устекинумаб у пациента с тяжелой формой псориаза.

Материалы и методы: проведен ретроспективный анализ случая с использованием истории болезни одного пациента, получавшего стационарное лечение в кожно-венерологическом отделении Городской больницы №2, Управления здравоохранением области Абай. Динамика состояния пациента отслеживалась через комплексную медицинскую информационную систему (КМИС) в период с 2011 по 2024 годы. Диагностические и лечебные процедуры проводились в соответствии с утвержденным клиническим протоколом Министерства здравоохранения Республики Казахстан №172 от 14 октября 2022 года. Публикация результатов лечения была разрешена руководством клиники и пациентом путем подписания информированного согласия.

Результаты: После добавления к стандартной противовоспалительной терапии препарата Стелара, состояние пациента значительно улучшилось. Препарат купировал такие симптомы как, кожный зуд, высыпания, болезненность в суставах. Согласно клиническим исследованиям устекинумаб продемонстрировал способность контролировать прогрессирование заболевания и улучшать качество жизни пациентов за счет снижения уровня провоспалительных цитокинов и модулирования противовоспалительных маркеров. Исследования также показали его эффективность в лечении симптомов псориатического артрита и его успех у различных групп населения, при этом 67,2% пациентов достигли PASI75 после двух доз.

Выводы: Данный клинический случай демонстрирует эффективность устекинумаба в лечении среднетяжелого и тяжелого псориаза, осложненного псориатическим артритом. Улучшение кожных поражений, симптомов в суставах и общего состояния пациента подтверждает потенциал биологической терапии в контроле заболевания и повышении качества жизни.

Ключевые слова: *псориаз, устекинумаб, биологические препараты, клинический случай.*

Түйіндеме

УСТЕКИНУМАБ: ПСОРИАЗДЫ ЕМДЕУГЕ АРНАЛҒАН ГЕНДІК - ИНЖЕНЕРЛІК БИОЛОГИЯЛЫҚ ПРЕПАРАТ-КЛИНИКАЛЫҚ ЖАҒДАЙ

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Кіріспе: Қазіргі дерматовенерологиядағы маңызды мәселелердің бірі-орташа және ауыр курсы бар псориазбен ауыратын науқастарды емдеудің тиімділігі мәселесі. Белгілі бір қабынуға қарсы цитокинді блоктау арқылы мақсатты әсерге бағытталған гендік-инженерлік биологиялық терапияны енгізу ауруды емдеу мәселелерінде айтарлықтай ілгерілеуге, сондай-ақ пациенттердің өмір сүру сапасын жақсартуға мүмкіндік берді.

Зерттеу мақсаты: псориаздың ауыр түрімен ауыратын науқаста устекинумаб препаратының клиникалық тиімділігін бағалау.

Материалдар мен әдістер: Абай облысының Денсаулық сақтау басқармасының № 2 қалалық ауруханасының тері-венерологиялық бөлімшесінде стационарлық ем алған бір пациенттің ауру тарихын пайдалана отырып, жағдайға ретроспективті талдау жүргізілді. Науқастың жағдайының динамикасы 2011-2024 жылдар аралығында кешенді медициналық ақпараттық жүйе (КМИС) арқылы бақыланды. Диагностикалық және емдеу рәсімдері Қазақстан Республикасы Денсаулық сақтау министрлігінің 2022 жылғы 14 қазандағы №172 бекітілген клиникалық

хаттамасына сәйкес жүргізілді. Емдеу нәтижелерін жариялауға клиника басшылығы мен пациент ақпараттандырылған келісімге қол қою арқылы рұқсат берді.

Нәтижелері: Стелара препаратын стандартты қабынуға қарсы терапияға қосқаннан кейін науқастың жағдайы айтарлықтай жақсарды. Препарат терінің қышуы, бөртпелер, буындардағы ауырсыну сияқты белгілерді тоқтатты. Клиникалық зерттеулерге сәйкес устекинумаб қабынуға қарсы цитокиндердің деңгейін төмендету және қабынуға қарсы маркерлерді модуляциялау арқылы аурудың дамуын бақылау және пациенттердің өмір сүру сапасын жақсарту қабілетін көрсетті. Зерттеулер сонымен қатар оның псориазды артрит белгілерін емдеудегі тиімділігін және әртүрлі популяциялардағы жетістігін көрсетті, пациенттердің 67,2% екі дозадан кейін PASI75-ке жетті.

Қорытынды: бұл клиникалық жағдай устекинумабтың псориазды артритпен асқынған орташа және ауыр псориазды емдеудегі тиімділігін көрсетеді. Терінің зақымдануын, буындардағы симптомдарды және науқастың жалпы жағдайын жақсарту ауруды бақылауда және өмір сапасын жақсартуда биологиялық терапияның әлеуетін растайды.

***Түйінді сөздер**: псориаз, устекинумаб, биологиялық препараттар, клиникалық жағдай.*

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Background

Psoriasis (Ps) is a chronic systemic immune-mediated disease of multifactorial origin, with genetic factors playing a predominant role [8]. It is characterized by hyperproliferation and impaired differentiation of epidermal cells, as well as an imbalance between pro-inflammatory and anti-inflammatory cytokines [19]. The pathological process extends beyond the skin, affecting the musculoskeletal system, endocrine organs, cardiovascular system, kidneys, and nervous system [20].

In most cases, Ps begins with the appearance of red papules on the skin, covered with silvery-white scales, which merge to form dense plaques ranging from 3 to 5 cm in diameter [2]. The global prevalence of Ps varies from 2% to 5%, predominantly affecting individuals of European descent [16]. In Kazakhstan, the prevalence is lower, with approximately 35 cases per 100,000 populations [23]. According to the Kazakh Scientific Center for Dermatology and Infectious Diseases, the highest prevalence rates in the country are reported in the East Kazakhstan, West Kazakhstan, and Kyzylorda regions [1].

As per clinical guidelines, the severity of Ps is assessed using the Psoriasis Area and Severity Index (PASI), which accounts for the degree of erythema, infiltration, scaling, and the area of skin involvement. A PASI score of <10 indicates mild disease, 11–30 signifies moderate severity, and >30 reflects severe disease. Treatment efficacy is defined as an improvement in the PASI score by 75% or more (PASI75) [12].

One of the most severe and frequent complications of Ps is psoriatic arthritis (PsA). PsA affects the distal and proximal joints of the hands, the spine, sacroiliac joints, nails, and entheses, eventually leading to patient disability [9].

Despite significant advancements in modern medicine, the treatment of moderate-to-severe Ps and PsA remains a considerable challenge. In some patients, satisfactory therapeutic outcomes are not achieved with conventional systemic anti-inflammatory drugs or tumor necrosis factor-alpha (TNFα) inhibitors [17]. However, the development of targeted therapies focusing on specific pro-inflammatory cytokines (or their combinations) offers a promising avenue to enhance treatment efficacy.

One such therapy is ustekinumab (UST; Stelara®), a genetically engineered biological agent (GEBA) comprising fully human immunoglobulin G1 kappa (IgG1κ) monoclonal antibodies (mAb) targeting human interleukin-12p40 (IL-12p40) [17]. This innovative treatment approach holds significant potential for improving outcomes in Ps and PsA management.

Objective of the study: to evaluate the clinical efficacy of ustekinumab in a patient with severe psoriasis.

Materials and Methods: A retrospective case analysis was conducted using the medical history of a patient who underwent inpatient treatment at the dermatology and venereology department of City Hospital No. 2, under the Health Administration of the Abay region. The patient's condition was monitored through the comprehensive medical information system (CMIS) from 2011 to 2024. Diagnostic and therapeutic procedures were performed in accordance with the clinical guideline approved by the Ministry of Health of the Republic of Kazakhstan (No. 172, dated October 14, 2022). The publication of treatment results was authorized by the clinic's management and the patient through the signing of an informed consent form.

Case description. Patient Z., born in 1997 (27 years old), has been under outpatient monitoring at the

dermatology department of Hospital #2 since October 2011. The most recent visit occurred in April 2021 due to a disease exacerbation and worsening of general health. Upon admission, the primary complaints included extensive skin eruptions on the scalp, trunk, and limbs; accompanied by severe itching, skin scaling, pain in the right shoulder and knee joints, swelling, and limited joint mobility.

Disease history: the diagnosis of psoriasis was first made at the age of 14, following the appearance of eruptions on the extensor surfaces of the elbows and knees, later spreading to the scalp. The lesions were characterized by red papules elevated above the skin, covered with whitish scales, accompanied by mild itching and occasional skin tightness. The patient initially sought care at a local clinic and was referred to a dermatologist. Exacerbations occur during the fall-winter season. Despite annual inpatient treatment, the patient does not adhere to discharge recommendations. In 2017, psoriatic arthritis was first diagnosed, and the patient was placed under the care of a rheumatologist. Treatment included Methotrexate (17.5–15 mg/week) in combination with folic acid and topical 2% salicylic ointment with "Betamethasone". Phototherapy was not administered due to the lack of necessary equipment. During subsequent disease exacerbations, the patient did not seek dermatological care or treatment. The patient was admitted to the inpatient department of Hospital #2 in February 2023.

Personal history: the patient's growth and development were age-appropriate. There is no history of viral hepatitis or skin diseases in childhood. Pulmonary tuberculosis was diagnosed in 2014. The patient began sexual activity at 17 years old, is currently married, and has an 8-year-old child. He lives in a well-maintained apartment under satisfactory material and living conditions. The patient smokes 7–10 cigarettes daily and consumes alcohol. He has a secondary technical education and works outside his specialty, often involving night shifts, cold exposure, and stressful conditions.

Allergic history: the patient reports an allergic reaction to cephalosporin medications.

Family history: positive for psoriasis, as the patient's paternal uncle is affected.

Objective examination: the patient is in moderately severe general condition. Consciousness is clear, and the patient is active. Height: 177 cm, weight: 58 kg (underweight). Body type: hyposthenic, proportional. No pathological changes in the head or face. Body temperature: 36.6°C. Lymph nodes: not enlarged. Cardiovascular, respiratory, and urinary systems: no abnormalities detected.

Local status: the dermatological condition is widespread and symmetrical, affecting the scalp, elbows, knees, trunk, shins, and thighs. The lesions include abundant lenticular and miliary papules of bright red color, covered with loose silver-white scales. Plaques measure up to 10 cm or more in diameter, flat, red, and raised above the skin surface, with irregular, scalloped edges and a hyperemic border. Skin texture is accentuated. Nail changes include deformity, thickening, yellow discoloration, transverse ridging, and pitting ("thimble sign"). The free edge of the nails is brittle. The "psoriatic triad" test is positive.

PASI Score: 90%. Figure 1 illustrates the findings.

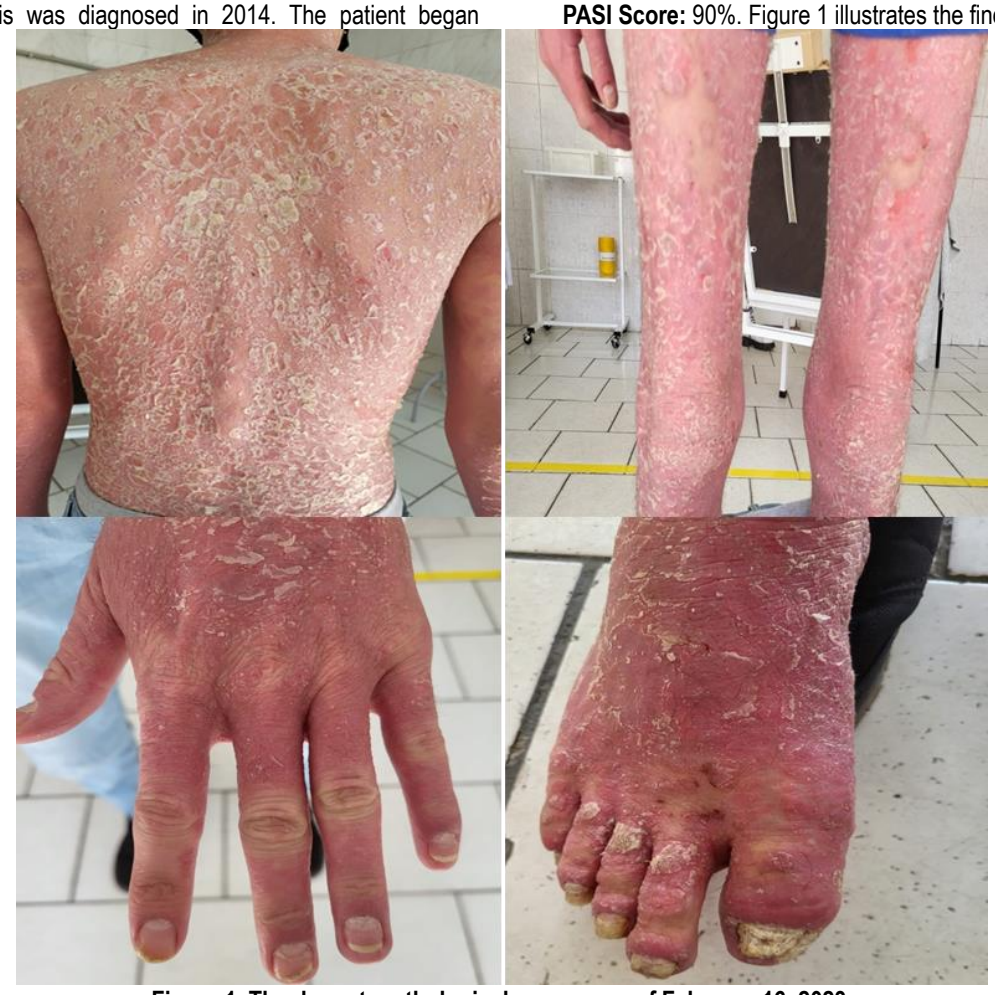

Figure 1. The dermatopathological process as of February 16, 2023.

Pain during palpation was noted in the thoracic and lumbar spine, as well as in the right shoulder and knee joints. The joints were not externally altered, but the range of motion was limited due to pain.

Laboratory findings. Complete blood count (17.02.2023):

hemoglobin – 136 g/L, erythrocytes – 4.8x10^{12}/L,
leukocytes – 9.1x10^{9}/L, lymphocytes – 22%,
monocytes – 3%, eosinophils – 2%,
band neutrophils – 2%, segmented neutrophils – 68%,
ESR – 18 mm/hour.

Conclusion: Signs of inflammation.

Blood test for RW (17.02.2023): Negative.

Urine analysis (17.02.2023): Color – straw yellow, pH – acidic, specific gravity – 1015, transparency – clear, protein – negative, glucose – negative, squamous epithelial cells – 2–4 per field of view, leukocytes – occasional per field of view, mucus – ++, bacteria – negative.

Conclusion: No pathology.

Biochemical blood analysis (17.02.2023): Total protein – 88 g/L, urea – 9.6 mmol/L, creatinine – 96 μmol/L, bilirubin – 16.80 μmol/L, cholesterol – 4.12 mmol/L, glucose – 4.8 mmol/L, AST – 18.10 U/L, ALT – 15.30 U/L.

Conclusion: No pathology.

Radiography of the joints (10.01.2023): Arthritis of the shoulder joints, Stage 1; arthritis of the knee joints, Stage 1; thoracic osteochondrosis.

Clinical diagnosis: Psoriasis, undifferentiated type, progressive stage, exacerbation. Psoriatic arthropathy. Functional class 2.

Treatment plan: Inpatient regimen. Diet: Table № 15.

Medication: Allergopress solution, 20 mg, intramuscular injection, once daily; externally – Novasalic ointment and 2% salicylic ointment applied thinly, twice daily; Stelara (ustekinumab) 45 mg/0.5 mL, subcutaneous injection. The second injection was administered four weeks after the first, followed by maintenance injections every 12 weeks (five injections per year).

Clinical outcome: After two injections, the patient reported an improvement in general condition, a reduction in skin lesions and scaling, and the resolution of joint pain (Figure 2).

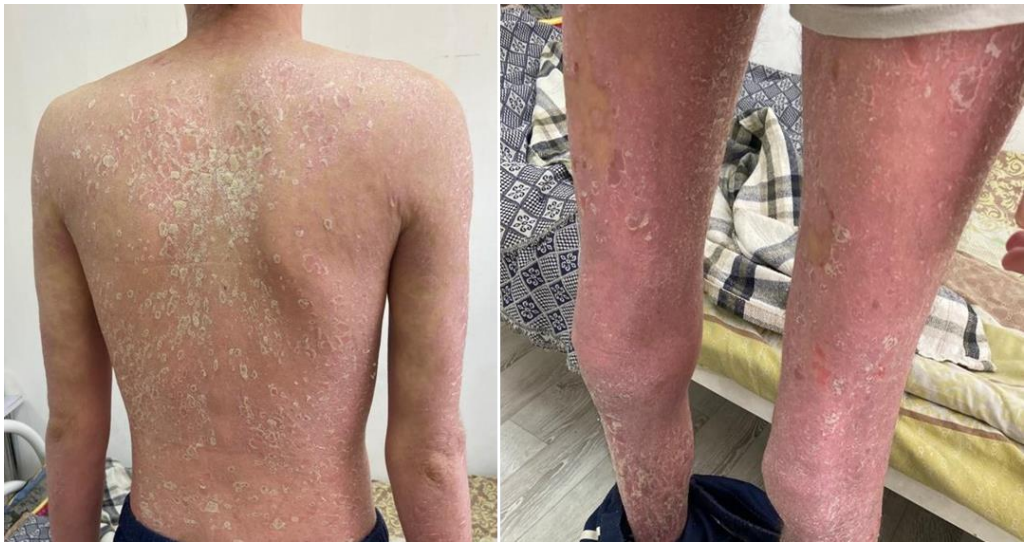

Figure 2. The dermatopathological process as of June 08, 2023.

As of the most recent visit (February 21, 2024), the patient reported no complaints. The skin pathological process was characterized by extensive areas of hyperpigmentation, with no papules, plaques, or scaling observed (Fig. 3).

Recommendations: Currently, the patient's treatment plan includes only the medication Stelara, as well as emollients for managing increased skin dryness. It is recommended that the patient undergoes monthly evaluations by a dermatologist and a rheumatologist to monitor symptoms dynamically and prevent potential complications.

Discussion

In recent years, ustekinumab, along with other biologic agents, has been increasingly utilized in the treatment of various autoimmune conditions [22]. *In vitro* and *in vivo* studies have demonstrated that this drug can reduce IL-12- and IL-23-mediated expression of skin-homing markers, activation proteins, and pro-inflammatory cytokines such as IFN-γ, IL-2, TNF-α, and IL-17A, which are elevated in Ps lesions. Additionally, it modulates the production of anti-inflammatory cytokines by decreasing IL-10 secretion and increasing IL-5 levels [4]. Numerous clinical trials have demonstrated that these medications not only control disease progression and severity but also significantly improve patients' quality of life [14, 15]. For example, the therapeutic efficacy of ustekinumab in treating moderate to severe Ps in patients over 18 years old has been established in two Phase III randomized, double-blind, placebo-controlled trials. The PHOENIX 1 study included 766 participants, where the first phase consisted of 12 weeks of placebo-controlled trials (ustekinumab was administered subcutaneously at doses of 45 mg/90 mg or placebo at weeks 0 and 4).

This was followed by a 28-week placebo-crossover phase (the first group continued to receive ustekinumab every 12 weeks, while the placebo group was switched to ustekinumab) and, finally, a 36-week randomized withdrawal phase (patients achieving PASI 75 at weeks 28 and 40 were re-randomized to continue ustekinumab or receive placebo until week 76).

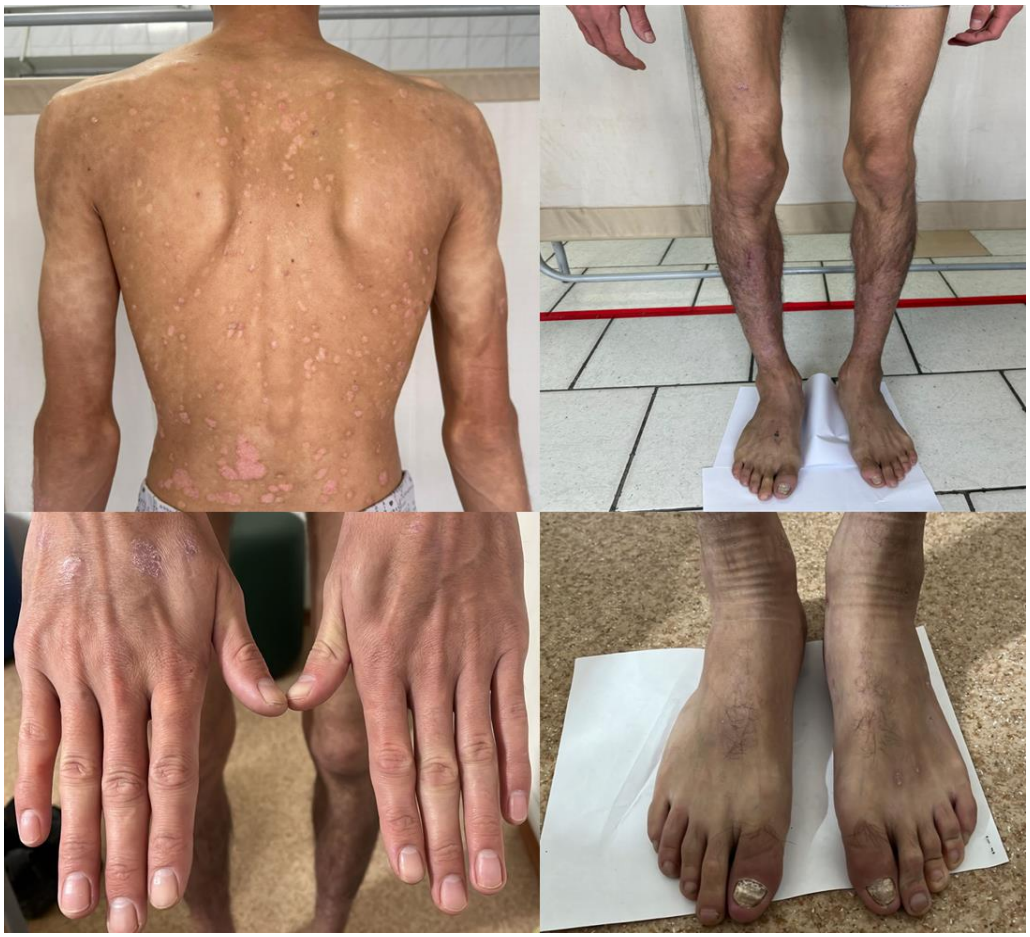

Figure 3. The dermatopathological process as of February 21, 2024.

The results showed a sustained therapeutic response and better clinical outcomes in patients receiving ustekinumab [14]. In the second study, PHOENIX 2, conducted in North America with 1,230 participants, the treatment phases were also part of Phase III trials. The key difference between PHOENIX 1 and PHOENIX 2 was that PHOENIX 2 investigated the potential to enhance treatment efficacy by reducing the dosing interval from 12 weeks to 8 weeks [15].

Another study focused on the efficacy and safety of ustekinumab therapy for Ps in individuals of Asian descent, specifically Taiwanese and Korean populations. According to the study results, 67.2% of patients achieved PASI75 after just two injections of the drug [21]. Additionally, several studies have noted that Stelara effectively addresses symptoms of PsA, alleviating joint tenderness and stiffness [3]. A summary of all key studies on the efficacy of ustekinumab in patients with Ps and PsA is presented in Table 1.

Table 1.

Overview of clinical trials of Ustekinumab in patients with psoriasis and psoriatic arthritis.

Author, Year	Research subject/type of wound/degree of lesion	Research Significance
1	2	3
Kauffman C.L. et al, 2004 [11]	A Phase 1 study conducted in 18 volunteers diagnosed with plaque psoriasis using intravenous injections administered at doses of 0.1 mg/kg, 0.3 mg/kg, and 0.5 mg/kg	67% of participants achieved a PASI75 response
Gottlieb A. et al, 2009 [5]	RCT involving 21 patients with plaque psoriasis using subcutaneous injections administered at doses of 0.27 mg/kg, 0.675 mg/kg, 1.35 mg/kg, and 2.7 mg/kg	75% of participants achieved a PASI75 response
Krueger G.G. et al, 2007 [13]	RCT involving 320 patients with moderate to severe psoriasis using treatment regimens with either a single course of 45 mg or 90 mg, or weekly dosing over 4 weeks	Improvement observed in up to 81% of participants
Gottlieb A.B. et al, 2007 [6]	RCT involving 146 patients with psoriasis and psoriatic arthritis using of 90 mg or 63 mg doses administered once a week within 4 weeks	42% of participants achieved a ACR20 response
Leonardi et al, 2008 [14]	RCT involving 766 patients with moderate to severe psoriasis using of 45 mg or 90 mg doses administered at weeks 0 and 4	67% of participants achieved a PASI90 response
Papp K.A. et al, 2008 [15]	RCT involving 1230 patients with moderate to severe psoriasis using of 45 mg or 90 mg doses administered twice a week within 12 weeks	Improvement observed in up to 76% of participants

Continuation of table 1.

1	2	3
Griffiths C.E. et al, 2010 [8]	RCT involving 903 patients with moderate to severe psoriasis using of 45 mg or 90 mg doses administered at weeks 0 and 4, repeating every 12 weeks	74% of participants achieved a PASI75 response
Igarashi A. et al, 2011 [10]	RCT was conducted with 158 patients with moderate-to-severe psoriasis, comparing ustekinumab 45 mg or 90 mg administered at weeks 0, 4, and every 12 weeks thereafter, to a placebo group that crossed over to ustekinumab treatment at week 12.	At week 12, 59.4% and 67.7% of ustekinumab 45 and 90 mg patients achieved PASI75
Tsai T.F. et al, 2011 [21]	A total of 121 patients with moderate-to-severe psoriasis received subcutaneous injections of ustekinumab 45 mg at weeks 0, 4, and 16, or placebo at weeks 0 and 4 followed by ustekinumab 45 mg at weeks 12 and 16.	By week 12, 67.2% of patients in the ustekinumab 45 mg group achieved a PASI 75 response.
Zhu X. et al, 2013 [24]	A total of 322 patients were randomly assigned to receive either ustekinumab 45 mg or a placebo at weeks 0 and 4, with those initially on placebo switching to ustekinumab at week 12.	By week 12, 82.5% of patients treated with ustekinumab achieved PASI 75 responses.
Ritchlin C. et al, 2014 [18]	RCT with 312 adults with active PsA: ustekinumab 45 mg or 90 mg (week 0, 4, q12 weeks) vs. placebo (week 0, 4, 16; crossover to ustekinumab 45 mg at week 24, 28, 40).	More ustekinumab-treated (43.8% combined) patients achieved ACR20 at week 24

Conclusion

This clinical case highlights the significant therapeutic potential of biological agents, particularly ustekinumab, in managing moderate-to-severe Ps complicated by PsA. The observed improvements in skin lesions, joint symptoms, and overall patient well-being underscore the efficacy of ustekinumab in controlling disease progression and enhancing quality of life. This case adds to the growing body of evidence supporting the use of targeted biological therapies as a cornerstone in the treatment of complex autoimmune conditions.

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