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Guselkumab cleared skin but failed to prevent progression of IgA nephropathy secondary to psoriasis: a case report and literature review

Abstract

Psoriasis is a chronic inflammatory skin disease associated with numerous comorbidities, including increased risk of psoriatic arthritis (PsA) in up to 30% of patients and kidney damage, which may eventually progress to end-stage renal disease (ESRD). The risk of developing chronic kidney disease (CKD) and ESRD is elevated, with odds ratios of 1.65 (95% CI, 1.29–2.12) and 1.37 (95% CI, 1.14–1.64), respectively. The following case is an example of a patient with generalized plaque psoriasis who, over the years, developed kidney damage due to IgA nephropathy (IgAN).

A 52-year-old female patient was admitted to the Clinic of Nephrology due to the exacerbation of IgAN, with a creatinine level of 2.8 mg/dL and an eGFR of 19 mL/min/1.73 m^2. The patient had suffered from chronic plaque psoriasis since the age of 15. At 38, she was diagnosed with sacroiliac joint involvement due to PsA. At that time, her creatinine level was 0.91 mg/dL. At 44, a decline in kidney function was noted (eGFR of 45.1 mL/min/1.73 m^2), and a kidney biopsy revealed moderately advanced, focal, sclerosing mesangial proliferative IgA glomerulonephritis with minimal, fresh extracapillary necrotic components and interstitial fibrosis of the renal cortex. It was suspected that the worsening of kidney function was related to the coexisting psoriasis. Therefore, the primary goal was to optimize psoriasis treatment.

For about 10 years, the patient was treated with methotrexate (MTX), which effectively controlled psoriasis, but her kidney function parameters continuously deteriorated. Between 2015 and 2023, a decline in eGFR from 45.1 to 37.1 mL/min/1.73 m^2 was observed. Due to the coexisting CKD, it was decided to discontinue MTX to avoid drug-related nephrotoxicity — at that time, her creatinine level was 1.52 mg/dl (eGFR 37.1 mL/min/1.73 m^2). As an alternative, systemic retinoid therapy was initiated to treat the underlying disease. Unfortunately, within a month, the treatment proved ineffective. In line with the current psoriasis treatment protocol, after exhausting conventional methods, the patient was offered biological therapy in April 2023.

In September 2023, after completing the proper qualification process, guselkumab, an antibody targeting IL-23 — a cytokine involved in the pathogenesis of psoriasis and other autoimmune diseases such as IgAN — was introduced. The therapy turned out to be highly effective in treating psoriatic skin lesions, but during the six-month follow-up, no improvement in kidney function was observed. Instead, further deterioration occurred, and the patient reached stage G4 of CKD (eGFR 19 mL/min/1.73 m^2).

This case demonstrates the need for early and regular monitoring of other organ functions in patients suffering from psoriasis. Therapy may result in effective skin clearing while failing to alleviate other extracutaneous psoriasis manifestations. When biological treatment is introduced, such as guselkumab, the deterioration of kidney function should be taken into account and prevented by strict monitoring.

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INTRODUCTION

Psoriasis is a chronic inflammatory skin condition affecting approximately 2.06% (95% CI, 0.61–6.58%) of the adult population in Poland [1]. While primarily known for its cutaneous manifestations, psoriasis is increasingly recognized as a systemic disease with potential implications for multiple organ systems [2]. Among these, kidney involvement has gained attention in recent years, with studies suggesting an increased risk of chronic kidney disease (CKD) [3]. The exact mechanisms leading to CKD in the context of psoriasis are not fully understood. Recently, attention has focused on shared immune cells involved in both inflammatory skin lesions and nephron dysfunction [3]. Additionally, psoriasis is thought to contribute to the gradual deterioration of endothelial function, leading to impaired kidney perfusion. The nephrotoxic effects may also result from the widespread, often long-term use of treatments for psoriasis and psoriatic arthritis (PsA).

Among patients with psoriasis, psoriatic nephropathy can be caused by various underlying conditions, including IgAN, focal segmental glomerulosclerosis (FSGS), and membranous nephropathy. The most commonly described psoriatic nephropathy is IgAN [14], as was the case described here. IgAN is the most common form of primary glomerulonephritis in Europe, affecting approximately 2.53 per 10000 patients across all age groups [4]. Although traditionally considered a distinct entity (primary IgAN), emerging evidence suggests a potential association between IgAN and psoriasis [5], possibly linked to shared inflammatory pathways [6]. The pathogenesis of secondary IgAN involves similar pro-inflammatory cytokines, with interleukin-23 (IL-23) playing a key role in psoriasis and regulating IL-17A [6], another crucial cytokine that triggers immune cells in this dermatitis [2]. The aforementioned cytokine intensifies the activity of lymphocytes and other immune cells, leading to the production of various pro-inflammatory and chemotactic proteins that drive inflammation in both the skin and kidneys [5]. This relationship underscores the complexity of systemic inflammation in psoriasis and highlights the need for comprehensive patient management. Consequently, these signaling pathways have become targets for new treatments aimed at interrupting these interrelated processes [2]. The risk of developing CKD and ESRD is elevated, with odds ratios of 1.65 (95% CI, 1.29–2.12) and 1.37 (95% CI, 1.14–1.64), respectively, and in addition, the severity of psoriasis is highly linked to a higher occurrence of CKD and ESRD [13].

In the treatment of generalized plaque psoriasis, both topical and systemic therapies are used. Depending on the severity of the disease and the clinical condition of the patient, treatment escalation occurs. The most commonly used systemic treatments include MTX, cyclosporine (CsA), and acitretin. The selection of appropriate therapy depends on the progression of this dermatosis, as well as additional factors such as comorbidities. However, in patients with moderate to severe plaque psoriasis for whom two of the aforementioned systemic treatments have proven ineffective and whose drug tolerance is limited, there is the possibility of offering them biological treatment with specific monoclonal antibodies targeting key interleukins involved in psoriatic pathogenesis, including TNF-α, IL-17, and IL-23.

Biologic therapies have revolutionized psoriasis treatment, offering unprecedented efficacy in skin clearance. Guselkumab, a monoclonal antibody targeting IL-23, has demonstrated remarkable effectiveness in treating moderate-to-severe plaque psoriasis [7, 8]. Moreover, it has been shown to be effective in patients with both psoriasis and PsA, especially in those with low PsA activity [8]. Studies indicate that guselkumab can provide consistent and lasting control of dermatological symptoms and low PsA activity [7]. However, its impact on other extra-cutaneous manifestations, particularly kidney complications, remains less well-defined. For patients who experience extra-cutaneous manifestations of psoriasis, such as kidney damage, it is worth considering whether deterioration in kidney function may affect the dosage of this medication and its pharmacokinetics. According to the Summary of Product Characteristics, no studies have been conducted to date that indicate a change in the pharmacokinetics of guselkumab in cases of kidney impairment. Additionally, deterioration of renal function is not an indication for discontinuation of this antibody.

This case report describes a patient with long-standing psoriasis who showed no improvement in joint pain (PsA) and additionally exacerbated IgAN, experiencing progressive kidney dysfunction despite achieving skin clearance with guselkumab therapy. By presenting this case, we aim to highlight the

complex relationship between psoriasis, PsA, IgAN, and biological treatment, emphasizing the possible dichotomy between skin and extracutaneous manifestations, as well as the importance of multidisciplinary care in managing patients with both dermatological and renal manifestations.

CASE REPORT

A 52-year-old female with IgAN was admitted to the Nephrology Clinic due to progressive deterioration of kidney function. Her serum creatinine was 3.07 mg/dL, and eGFR was 16 mL/min/1.73 m^2. The urinary albumin-to-creatinine ratio (UACR) was 2297.02 mg/g. Her medical history included generalized plaque psoriasis, PsA, asthma, hypertension, and biopsy-confirmed IgAN (2015). She was treated with biological therapy (guselkumab) targeting IL-23 since September 2023. The patient reported regular use of antihypertensive medications, including indapamide, telmisartan, and amlodipine. During the last hospitalization, in April 2024, SGLT2 inhibitor therapy (flozins) was initiated.

In Table 1 and Figure 1, we present some important facts from the patient's medical history, which are described more precisely below.

Table 1. Chronology of the therapy and clinical course focused on skin, joint, and kidney psoriasis involvement

Year	Patient's age	Creatinine/eGFR (mg/dL)/ (mL/min/1.73 m^2)	Proteinuria (g/L)	Clinical course (comorbidity, therapy)	
1986	15	–		Psoriasis	
2009	38	0.91/83	1.89	PsA	MTX
2013	42	1.0/72			
2015	44	1.4/45.1		Biopsy: IgAN	
2017	46	1.7/37	0.14		
03.2023	51	1.52/37.1			Acitretin
04.2023	51	1.46/40.1			
10.2023	51	2.25/25			Guselkumab
11.2023	51	2.37/23			
04.2024	52	2.8/19	3.03		
06.2024	52	2.5/22	1.89		

CKD-EPI — Chronic Kidney Disease Epidemiology Collaboration; eGFR — estimated glomerular filtration rate; MTX — methotrexate

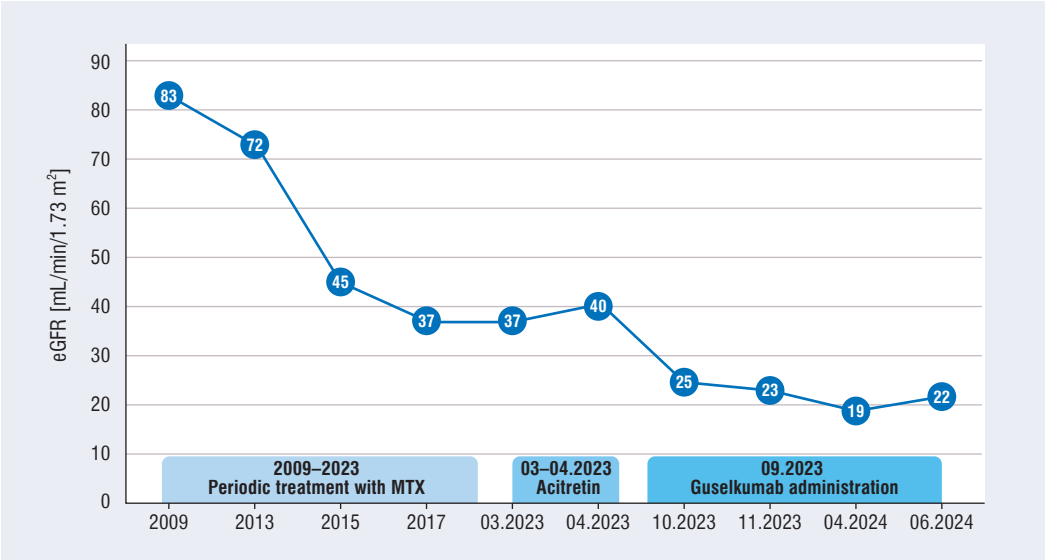

Figure 1. Estimated glomerular filtration rate (CKD-EPI) before and during treatment with guselkumab

She was diagnosed with plaque psoriasis at age 15, and she was initially managed with topical treatments and occasional MTX. At the age of 38, she was diagnosed with hypertension and persistent lumbosacral spine pain that led to the PsA diagnosis after sacroiliitis was detected on X-rays. Additionally, a 24-hour urine sample revealed significant protein loss at a level of 3.21 g per day. The kidney biopsy showed moderately advanced IgAN with focal scarring and a small necrotic component, suggesting a possible link between psoriasis, PsA, and kidney function decline. She received a two-week course of prednisone, and ramipril was introduced for nephroprotection and to treat hypertension.

Two years later, her eGFR decreased to 45.1 mL/min/1.73 m^2 (CKD stage G3a A2). Despite papular psoriasis lesions, MTX dosage was not increased due to potential drug nephrotoxicity. Ultraviolet B (UVB) phototherapy and topical treatments were prescribed, and she was given medical follow-up.

At the age of 46, she experienced a decline in kidney function to eGFR 37 mL/min/1.73 m^2. The second biopsy results showed moderately advanced, focal scarring, mesangial proliferative IgAN (Oxford Classification scores: M1, E1, S1, T1) with a small, fresh necrotic extracapillary component. Moderate, focal tubular atrophy and interstitial fibrosis of the renal cortex with mild arteriolosclerosis were also noted. The medical team hypothesized that the kidney function decline was related to the coexisting psoriasis and PsA, leading to a two-week course of prednisone treatment. After completing steroid therapy, the patient was prescribed MTX at a dose of 7.5 mg weekly, and due to the diagnosis of hypertension, ramipril at a dose of 20 mg daily was initiated. One year later, she was hospitalized for cervical cancer, undergoing a total hysterectomy with complications including sigmoid wall perforation and massive adhesions.

By early 2023, she presented with exacerbated psoriasis skin lesions and an eGFR of 37.1 mL/min/1.73 m^2. MTX was continued, but due to flare-ups and comorbidities, treatment with acitretin (20 mg daily) and UVB phototherapy were recommended. When this failed, she was re-hospitalized, and biological treatment with guselkumab was initiated in September 2023.

Post-treatment, she experienced abdominal pain and diarrhea and was diagnosed with ileitis, with an eGFR of 23 mL/min/1.73 m^2. Due to chronic inflammatory disease (PsA) and elevated serum amyloid level (SAA) — 26.9 mg/l, amyloidosis was suspected but ruled out by a fat biopsy. Guselkumab improved her psoriasis skin lesions very effectively but did not enhance renal function or alleviate joint pain. The 7-month change in eGFR showed a decline of 6 mL/min/1.73 m^2, with persistent substantial proteinuria.

DISCUSSION

Psoriasis is a chronic inflammatory skin disease and autoimmune disease [5], characterized by excessive keratinocyte activation and proliferation. One of the most known extra-cutaneous psoriasis manifestations, PsA, affects up to 30% of psoriasis patients and is a chronic inflammatory disease classified as seronegative arthritis. In both conditions, genetic factors, particularly the *HLA-C*06* gene, combined with environmental triggers, increase the risk of disease development and exacerbation. Key pro-inflammatory proteins involved include IL-17A, IL-23, and TNF-α, which are targets for biological treatments of both conditions [2, 5, 6].

Furthermore, psoriasis is associated with more serious comorbidities, such as obesity, hypertension, cardiovascular diseases, arthritis, and kidney damage, potentially leading to CKD and ESRD [2, 3, 10, 11]. Several contributing factors necessitate regular monitoring of kidney function in psoriasis patients through biochemical tests to detect early decline and minimize risk factors. Among the kidney conditions associated with psoriasis, IgAN is the most common.

Various mechanisms may underlie renal function deterioration in psoriasis [12]. Chronic inflammation, driven by vascular endothelial damage [13], can lead to atherosclerosis and nephron damage from impaired blood flow. Th17 lymphocytes play a key role by producing IL-17A, which stimulates immune activity and causes inflammation in the glomeruli, leading to fibrosis and nephron damage. Psoriasis-related IgAN may result from the fact that both psoriasis and IgAN share similar immune pathways involving Th2 and Th17 responses, with IL-23 being crucial in both conditions [5].

IgAN is characterized by the formation of abnormal IgA antibodies (galactose-deficient IgA1, Gd-IgA1) [14]. In psoriasis, IL-23 may stimulate the production of these defective antibodies. The immune system then generates

autoantibodies against Gd-IgA1, forming immune complexes that deposit in the renal glomeruli [11]. These deposits trigger complement system activation and immune cell recruitment, leading to local inflammation and irreversible nephron damage.

Medications are another factor contributing to CKD development in patients with psoriasis [13]. Drugs like MTX and CsA are commonly used to treat moderate-to-severe psoriasis; unfortunately, they can impair kidney function. MTX can lead to kidney damage through intratubular precipitation, while CsA affects renal perfusion and exacerbates nephron inflammation. Additionally, secondary amyloidosis associated with MTX and CsA may contribute to kidney failure. However, current evidence suggests that MTX and CsA do not consistently cause kidney failure in psoriasis patients. Consequently, balancing psoriasis control and renal health becomes challenging.

The clinical presentation of IgAN often includes painless hematuria and mild proteinuria. As the disease progresses, a gradual decline in the glomerular filtration rate can lead to irreversible CKD. Treating IgAN in the context of psoriasis requires careful therapeutic management. Controlling psoriasis activity is essential, as more severe disease activity correlates with a higher risk of kidney damage. Integrated care addressing both skin and kidney health is crucial for optimizing patient outcomes and minimizing irreversible renal damage [10].

CLINICAL SUMMARY

Our clinical case demonstrates that psoriasis, a chronic inflammatory disease, is a complex immunological process that can lead to damage in various tissues and organs, including joints (PsA) and kidneys (IgAN) [2, 6]. Despite shared pathogenic pathways between psoriasis and secondary IgAN leading to CKD [12], guselkumab has proven effective only in treating psoriasis [7], underscoring the complexity of managing both conditions.

Veronesi *et al.* analyzed the change in renal function in 92 psoriasis patients who did not respond well to systemic therapies (the majority treated previously with CsA and/or MTX) and were switched to biologics, including anti-IL-12/23 monoclonal antibodies in the case of 25% of patients [9]. Over a year, a decrease in serum creatinine level was observed in 87% of patients. The mean serum creatinine decreased substantially from 0.98 to 0.9 mg/dL. Despite the values being within the normal range, an improvement in kidney function was noticeable in patients with psoriasis. The authors did not observe significant differences between the effects of anti-TNF-α, anti-IL-17, and anti-IL-12/23 biologics on creatinine levels. These results suggest that similar immunological mechanisms may occur in the unclear, complex pathogenesis of both conditions.

In the presented case, MTX was used for over 10 years, but due to worsening kidney function, dose increases were not possible. Given the patient's hypertension, CsA was avoided, and acitretin was recommended, though it was not fully effective in controlling skin lesions. At the time of CKD diagnosis (2015), due to IgAN, the patient's eGFR was 45.1 mL/min/1.73 m^2. By September 2023, when guselkumab was initiated, the GFR had decreased to 40.1 mL/min/1.73 m^2. Despite effectively managing skin lesions, guselkumab did not improve kidney function. In April 2024, the patient was hospitalized for worsening kidney function (GFR of 19 mL/min/1.73 m^2, elevated UACR of 2292.02 mg/g creatinine, and hematuria), indicating limited effectiveness of biological treatment in this secondary IgAN case.

Up to date, only one case report described guselkumab-induced kidney injury [15]. Since guselkumab inhibits IL-23, which stimulates Th-17 lymphocytes involved in autoimmune diseases, the development of kidney disease is counterintuitive. Stryckers *et al*. observed nephrotic syndrome due to FSGS that developed 2 weeks after introduction of guselkumab and resolved after cessation of the drug without relapse for 2 years in a male patient with chronic plaque psoriasis resistant to standard therapy. Interestingly, a kidney biopsy revealed IgA deposits in the mesangium; however, no other indicators of IgAN were observed. FSGS was diagnosed using electron microscopy. Discontinuing guselkumab, which correlated with the recurrence of skin lesions, led to improved kidney function, suggesting the guselkumab-induced secondary FSGS [15].

Both our and the abovementioned cases underscore the importance of a comprehensive approach to managing psoriasis, particularly monitoring the function of other organs, such as the kidneys. They highlight the presence of extracutaneous complications of psoriasis and emphasize that kidney function assessments

should be conducted regularly, especially in patients with moderate to severe disease activity. According to many authors, special monitoring should be provided for patients with psoriasis affecting more than 3% of body surface area and those taking potentially nephrotoxic medications [10]. The use of nephrotoxic drugs should also be avoided in patients with impaired kidney function, and drugs such as CsA should not be used for more than two years [10]. Key parameters that should be monitored in patients undergoing systemic psoriasis therapy include urine albumin levels, creatinine, and eGFR. These measures highlight the crucial role of dermatologists and nephrologists in spreading knowledge about psoriasis comorbidities [10], which allows for early detection of patients at risk of irreversible kidney damage.

Collaboration between dermatologists and nephrologists is crucial to prevent irreversible kidney damage and improve patient outcomes.

CONCLUSIONS

This case demonstrates the complexity of psoriasis in terms of disease progression, comorbidities, and the selection of a therapy that is both effective and safe. Early and regular monitoring of other organ functions, particularly the kidneys, is crucial to prevent further damage and avoid ESRD progression. Therapy may result in effective skin clearing while failing to alleviate other extra-cutaneous psoriasis manifestations. When biological treatment is introduced, such as guselkumab, the deterioration of kidney function should be taken into account and prevented by strict monitoring.

ARTICLE INFORMATION AND DECLARATIONS

Ethics statement:

Informed consent was obtained from the patient.

Author contributions:

Collection of medical data: J. R., F. K., P. S.
Manuscript writing: D. S., J. R.
Article revision: A. D.-S., F. K., P. S.

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Conflict of interest:

Authors have nothing to declare.

Supplementary material:

None.

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