Betamethasone dipropionate and calcipotriol foam as an adjuvant therapy in patients with severe psoriasis treated with biologic drugs

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ABSTRACT

Introduction: Introduction of novel biologic treatments for plaque psoriasis has revolutionized treatment approach and improved outcomes in patients with moderate-to-severe disease. New groups of biologics are even more effective and better tolerated compared to their predecessors. However, none of the currently available biologic drugs is associated with complete skin clearance in all treated patients. Moreover, the requirement to stop therapy in accordance with previous therapeutic program guidelines in Poland may have contributed to a gradual loss of efficacy of biologic drugs. Betamethasone dipropionate (BD) and calcipotriol (CAL) foam is the most widely studied topical drug in the therapy of mild forms of psoriasis. Numerous clinical trials have demonstrated its excellent efficacy not only in reactive therapy but also in preventing recurrences through the implementation of proactive therapeutic regimens.

Case reports: We present 2 cases of patients with severe psoriasis and psoriatic arthritis who were treated with biologic drugs with incomplete remission of skin lesions. Topical therapy with BD/CAL foam was introduced to treat refractory psoriatic lesions, leading to excellent outcomes.

Conclusions: The reported cases show that therapy with BD/CAL foam may be an effective adjuvant treatment of psoriasis in cases of incomplete and unsatisfactory response to systemic therapies, including biologics.

Key words: psoriasis, biologic treatment, topical treatment.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease with an estimated prevalence of 1–3% of the global population. In recent years, there has been a growing awareness of the systemic nature of the condition, which is associated with multiple comorbidities, particularly metabolic syndrome and cardiovascular complications. A holistic approach to patients with psoriasis also requires an evaluation of disease impact on the quality of life and consideration of the negative psychosocial effects of the disease [1].

Most patients with psoriasis experience mild forms of the disease, with skin lesions occupying less than 10% of the body surface and having no substantial adverse impact on the quality of life. In this group, topical medications are usually adequate for treatment [2]. Combination formulations containing betamethasone dipropionate (BD) and calcipotriol (CAL) are the most extensively researched and effec-

tive topical agents for psoriasis [3]. The most recently approved BD/CAL foam formulation, benefiting from the phenomenon of supersaturation, is reported to have even higher efficacy. Furthermore, it has been studied and approved for longterm proactive therapy to prevent disease relapse [4]. One of the studies published "of late" found that topical treatment with BD/CAL foam significantly reduced the expression of memory cell markers including CD4, CD8, CD103, CD69, CD49, and CXCR6 in psoriatic skin biopsy specimens after 12 weeks. The observations were made primarily in the epidermis and, to a lesser extent, in the dermis. This is likely attributable to the fact that BD/CAL foam targets the epidermis and has a limited penetration into the dermis. The findings of the study support the efficacy of BD/CAL foam in preventing disease relapses, which are mainly mediated by memory cells [5].

Over the last two decades, there has been enormous progress in the systemic treatment of psoriasis with biologic agents. Drugs in this group work by inhibiting specific proinflammatory cytokines that are implicated in the pathogenesis of the disease. Biologic agents gradually have changed the efficacy expectations from PASI50 to PASI75 (drugs targeting the tumor necrosis factor (TNF)-α and interleukin (IL)-12/23), and to PASI 90 and PASI100 (IL-17 and IL-23 inhibitors) [6].

However, despite the excellent efficacy of biologics, in a proportion of patients undergoing this type of treatment, psoriatic lesions may persist, requiring additional therapeutic interventions. According to the Polish therapeutic guidelines, topical medications should be used as the primary therapy for patients with mild forms of psoriasis. In individuals with moderate to severe disease, topical therapies are recommended as an adjunct to systemic treatment and phototherapy [7].

OBJECTIVE

We present 2 cases of patients treated with biologic agents who received adjuvant therapy with BD/CAL foam.

CASE REPORTS

Case 1

The case involved a 55-year-old male patient with no addictions and a history of severe plaque psoriasis since the age of 18. In addition, the patient had experienced pain in the peripheral joints for 12 years, diagnosed as psoriatic arthritis (PA). The patient's comorbidities included grade 3 obesity, hypertension, and dyslipidemia. The man received systemic treatment for psoriasis, initially with subcutaneous methotrexate at a dose of 20 mg/week. However, the medication was discontinued because of poor tolerance (abdominal symptoms) and a lack of improvement after 4 months of therapy. Subsequently, the patient was enrolled in a clinical trial of ixekizumab; however, the treatment was stopped after 1 month because of headaches with accompanying blood pressure elevation. Following the addition of cyclosporine, the patient reported nausea, increased sweating, and abdominal pain. For this reason, cyclosporine treatment was discontinued as well.

In view of the severe clinical course of psoriasis and the inefficacy of systemic therapies with cyclosporine and methotrexate, the patient was included in the National Health Fund (*Narodowy Fundusz Zdrowia*

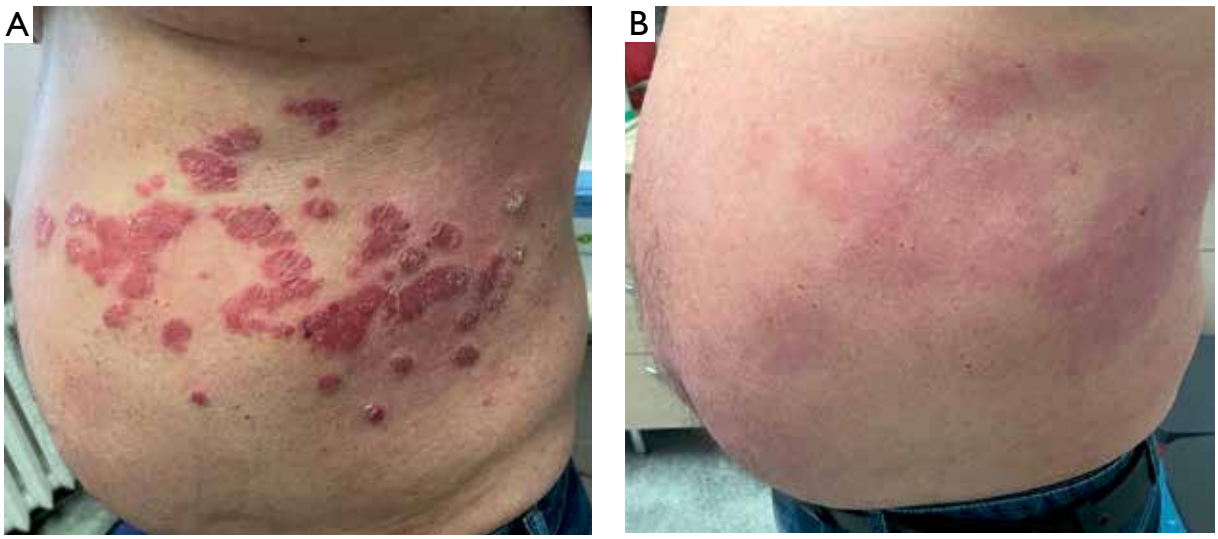

Figure 1. Psoriatic lesions on the abdominal skin in Patient 1: before (**A**) and after (**B**) treatment with BD/CAL foam

– NFZ) drug program to receive biologic treatment with ixekizumab. The patients had very good tolerance throughout the first 96-week course of therapy, with complete resolution of psoriatic lesions. However, following a pause in treatment mandated by the requirements of the drug program, there was a recurrence of skin lesions, validating the patient's resumption of treatment. Ixekizumab was reintroduced, but the efficacy of the drug was lower during the second course of treatment, with refractory psoriatic plaques persisting on the abdominal skin at week 16 of therapy (fig. 1 A). BD/CAL foam was added to the treatment regimen as an adjuvant therapy, to be applied once daily for 4 weeks. Complete resolution of skin lesions was achieved (fig. 1 B).

Case 2

The case involved a 68-year-old male patient with no addictions and a history of psoriasis vulgaris (diagnosed in 1992) and severe PA (diagnosed in 2005). The patient's comorbidities included hypertension, hepatic steatosis, grade 1 obesity, and status post laparoscopic cholecystectomy for cholelithiasis. In 2011, the patient completed a course of rifampicin and isoniazid for latent tuberculosis (as part of chemoprophylaxis). The man also had a history of systemic antipsoriatic therapies, including acitretin and PUVA therapy, with no improvement in his skin condition. Following the diagnosis of PA, the man was treated with methotrexate at doses ranging from 20 to 10 mg (the dose was reduced because of symptoms of intolerance, including nausea, vomiting, and hair loss). After an attempt was made to introduce cyclosporine, the patient developed marked symptoms of drug intolerance after the first dose, with significant elevations in blood pressure and sternal and epigastric pain.

The patient was assessed as eligible for treatment with etanercept, which he had been taking intermittently since 2011, as part of the drug program for the treatment of

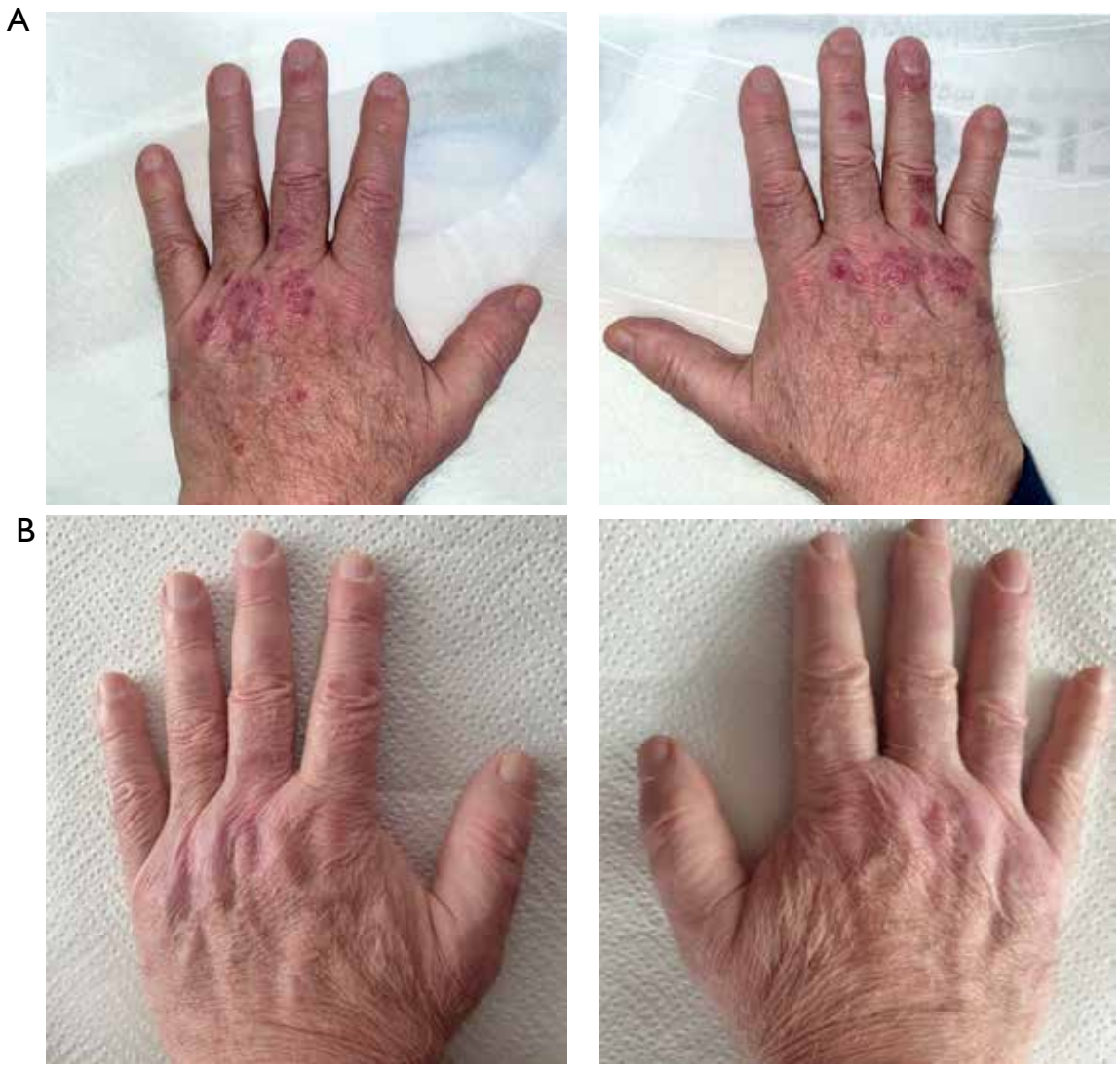

Figure 2. Psoriatic papules and plaques on the dorsal surfaces of hands in Patient 2: before (**A**) and after (**B**) adjuvant treatment with BD/CAL foam

aggressive PA. Biologic therapy manages the patient's joint symptoms successfully; however, its efficacy is comparatively lower in addressing skin lesions, which have a tendency to worsen over time. According to the patient, psoriatic plaques on the dorsal surfaces of the hands were particularly bothersome (fig. 2 A). Topical treatment with BD/CAL foam was initiated as adjuvant therapy, resulting in a complete remission of psoriasis.

DISCUSSION

Topical therapies are the first-line treatment option for 70–80% of patients diagnosed with mildtomoderate psoriasis. In clinical practice, BD/CAL combination formulations are the most commonly prescribed topical medications across various European countries, including Germany, the UK, and Spain [7]. By adding calcipotriol, a vitamin D analogue, synergy is is achieved with the glucocorticosteroid, enhancing its potency. Also, calcipotriol reduces the risk of local adverse effects of the glucocorticosteroid and the probability of lesion recurrence upon drug discontinuation [3]. BD/CAL combination formulations are characterized by the highest efficacy of all available topical drugs and are convenient to apply. This directly contributes to improved patient adherence and compliance, which are crucial for therapeutic success.

In a proportion of patients with moderate and severe psoriasis who exhibit contraindications to systemic therapies, intolerance of treatment, or have concerns about adverse effects, topical medications with BD/CAL may serve as a viable alternative. Data available in the literature focus mainly on BD/CAL foam, which is considered to be the most potent formulation in this group [8]. The efficacy of the drug in this patient population is discussed in a recently published literature review; practical recommendations have also been formulated [9].

The approval of the first biologic drugs in early 21st century marked the beginning of a new era in the treatment of patients with moderate to severe plaque psoriasis. Because of high therapeutic efficacy of these agents, expected treatment outcomes were defined as a decrease in baseline PASI values by 90% to as much as 100%, which, in practice, corresponds to complete or nearcomplete skin clearance [10]. Despite the unquestionably high efficacy of biologic drugs, complete remission of psoriatic lesions does not occur in all treated patients. For some patients, residual psoriatic plaques persist, which can significantly affect the quality of life and require additional topical therapies. Crucially, for optimal treatment efficacy, biologics should be used on a longterm basis and without interruption. Once initiated, biologic therapy should not be discontinued if it proves to be effective and welltolerated by the patient [11]. A recently published systematic review of reports on the discontinuation of biologic therapy shows that interrupting therapy with infliximab, etanercept, and secukinumab is associated with poorer therapeutic outcomes during the second course of treatment [11].

In Poland, uninterrupted biologic therapy can be provided exclusively with older biologic drugs with anti-TNF-α action. For newer drug groups, an additional request of the treating physician is a mandatory prerequisite. In the past, all therapies had to be interrupted, initially after only 48 weeks, and later after 96 weeks of treatment. Consequently, a large number of patients undergoing therapy within NFZ's drug programs for many years have experienced interruptions in treatment on one or even several occasions. Some of these patients experience adverse effects of treatment interruption, such as impaired therapeutic efficacy and persistence of skin lesions.

Both patients presented above had undergone intermittent biologic therapy. Patient 1 was treated with ixekizumab, which is one of the most effective biologic agents currently available, while Patient 2 received etanercept, which is considered the least effective biologic drug. In both patients, response to treatment decreased over time, and persistent skin lesions, despite meeting the criteria for adequate improvement defined in the drug program, had a considerable negative impact on their quality of life. As a result, an additional therapeutic intervention was required. The interventional treatment regimen based on BD/CAL foam turned out to be effective and led to complete resolution of skin lesions.

CONCLUSIONS

Biologic therapies, while undeniably the most effective among all available psoriasis treatments, do not achieve complete efficacy in 100% of treated patients. BD/CAL foam is a very good option for adjuvant therapy in patients with suboptimal therapeutic responses to biologic drugs.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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