Generalised pustular psoriasis – a case report and review of therapeutic approaches

Ciężka, uogólniona łuszczyca krostkowa – opis przypadku i krótki przegląd piśmiennictwa

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ABSTRACT

Introduction. Generalised pustular psoriasis (GPP) is regarded as a rare clinical subtype of psoriasis. The severity of GPP varies from a benign, chronic course to severe and widespread, life-threatening disease. Due to the uncommon nature of GPP, establishing treatment guidelines for this variant of psoriasis is challenging.

Objective. To present the case of a patient with GPP with a short review of therapeutic approaches.

Case report. Our patient was treated with standard methods such as acitretin, then cyclosporine and methotrexate as well as with biologic drug – infliximab. During the last and the most severe flare, combination therapy with systemic retinoid and PUVA (Re-PUVA) was used.

Conclusions. The treatment in GPP should be determined individually according to the severity of the disease, age, gender and comorbidities, as well as according to the physician's experience with particular methods and their side effects. In addition, the availability of therapeutic options should be taken into consideration.

STRESZCZENIE

Wprowadzenie. Łuszczyca krostkowa jest odmianą kliniczną łuszczycy, której przebieg może być bardzo ciężki i zagrażać życiu. Ze względu na rzadkość schorzenia ustalenie pewnych standardów leczenia okazuje się bardzo trudne.

Cel pracy. Przedstawienie przypadku ciężkiej, uogólnionej łuszczycy krostkowej wraz z krótkim przeglądem piśmiennictwa dotyczącego możliwości leczenia.

Opis przypadku. Pacjent był leczony zarówno dostępnymi metodami standardowymi, obejmującymi acytretynę, cyklosporynę A i metotreksat, jak i lekiem biologicznym – infliksymabem. Podczas ostatniego, najcięższego zaostrzenia zastosowano acytretynę w połączeniu z fotochemioterapią PUVA – RePUVA.

Wnioski. Wybór metody leczniczej powinien zależeć ściśle od ciężkości stanu klinicznego, wieku pacjenta i chorób współistniejących. Doświadczenie lekarza i dostępność danego leku to również bardzo ważne cechy determinujące sposób leczenia.

INTRODUCTION

Generalised pustular psoriasis (GPP) is regarded as a rare clinical subtype of psoriasis, characterised by the occurrence of sterile, sub-corneal pustules with concomitant fever and lymphadenopathy. It is also known as von Zumbusch psoriasis. The severity of GPP varies from a benign, chronic course to severe and widespread, life-threatening disease [1–3].

OBJECTIVE

The aim of this paper is to present a severe GPP case and a short review of existing guidelines and novel therapeutic approaches.

CASE REPORT

A 31-year-old male patient suffering from psoriasis since early childhood was admitted to the Department of Dermatology in February 2014 due to the exacerbation of skin lesions, with pustular eruption involving almost the whole body surface.

Family history of psoriasis was negative. At the beginning the course of the disease was stable with psoriatic skin lesions limited to the predilection sites. Joint pain was never noted. In 2009, limited pustular lesions overlapping typical psoriatic plaques were observed for the first time. He was hospitalised and the treatment with acitretin in an initial dose of 50 mg/day was introduced. The clinical response was very good; after 2 months he was almost clear, and the dose of acitretin was reduced. However, after 6 months, due to elevation of triglycerides, this treatment had to be discontinued. During the next relapse, methotrexate administered orally in weekly doses of 15–7.5 mg was used and brought the benefit up to 1.5 years. In 2011 he was qualified for treatment with infliximab, which was successfully used up to 1 year (6 injections). In May 2013, gradual worsening of skin condition with pustule formation led to hospitalisation and introduction of cyclosporine in an initial dose of 5 mg/kg. Despite the good clinical response, the dose needed to be reduced, and consequently the therapy had to be stopped due to elevation of creatinine level.

During an actual flare, skin lesions were extensive, erythematous with pustules and were accompanied by general symptoms such as malaise, chills and fever up to 39° (Figure 1). Blood tests revealed leukocytosis, elevated erythrocyte sedimentation rate and C-reactive protein while aminotransferases, creatinine levels, and lipid profile were within normal values. He was treated with a wide range of antibiotics and short pulses of systemic kortykosteroids, replaced, after exclusion of contraindications, with systemic retinoid (75 mg/day of acitretin). This time the skin lesions were more recalcitrant and the response was not rapidly noticed. After reducing the dose of acitretin, PUVA therapy was added. Combined treatment with retinoid and PUVA (Re-PUVA) was continued up to 20 irradiations and brought complete clearance of skin lesions, although lipid levels started to increase again.

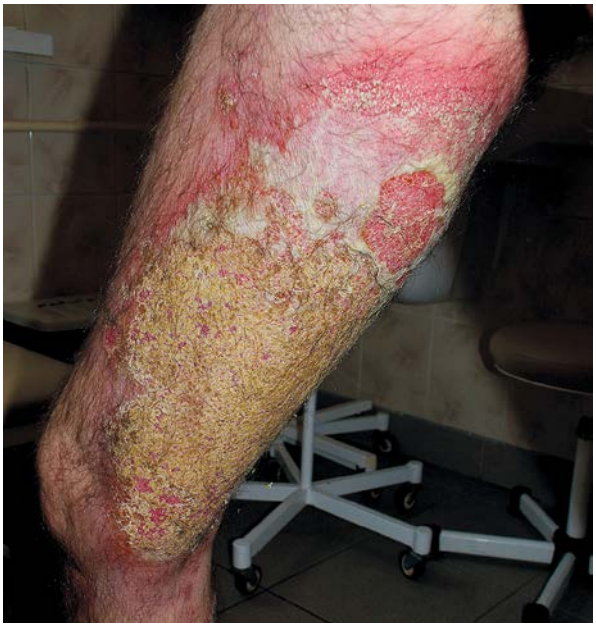

Figure 1. Generalised pustular psoriasis (courtesy of Prof. Ryszard Żaba)

Rycina 1. *Uogólniona łuszczyca krostkowa (dzięki uprzejmości prof. dr. hab. med. Ryszarda Żaby)*

DISCUSSION

Standard therapy

Due to the uncommonness of GPP, and only single case reports and short case series published in the literature, establishment of treatment guidelines for this variant of psoriasis is challenging. The standard therapy involves, as first choice, the vitamin A derivative acitretin, then cyclosporine and methotrexate as well as photochemotherapy – PUVA [1–3].

All above-mentioned forms of treatment were used in our young patient. Acitretin, cyclosporine and methotrexate brought transient improvement but also typical side effects. During the last, more severe flare, oral corticosteroids were used at the beginning and then were replaced with systemic retinoid again. Systemic corticosteroids generally are not recommended in GPP because of the risk of rebound phenomenon flares after reducing the dose or drug withdrawal; however, a recent literature review by German authors [4] revealed a lack of studies confirming this risk. Clinical experience suggests

that the risk of the withdrawal effect may be reduced by combination of corticosteroids with another systemic agent which will be continued after their cessation [4]. Some other authors justify their usage in cases of severe GPP-related pneumonitis and acute respiratory distress syndrome (ARDS) [5]. Moreover, systemic corticosteroids beside cyclosporine and infliximab are still regarded as first line therapy for impetigo herpetiformis – GPP in pregnancy [3]. The second cycle of monotherapy with acitretin in our patient also did not bring a marked improvement, which is why PUVA was added. Re-PUVA (combination therapy with systemic retinoid and PUVA) seems to be more effective; the clinical response is faster and the total dose of necessary UVA is lower. The safety profile due to the anti-cancerogenic effect of retinoids is also better than PUVA alone [1, 3, 6, 7].

Biologic therapy

The efficacy of biologic therapy in different immune-mediated inflammatory diseases, including resistant types of plaque psoriasis and psoriatic arthritis, is well documented. The studies resulted in formulation in 2009 of European guidelines on treatment of psoriasis vulgaris [8]. The first biological agent was approved for the treatment of psoriasis in 2004. According to these guidelines, biologicals are recommended for the treatment of moderate to severe forms of psoriasis (PASI > 10) in patients in whom phototherapy or standard systemic therapy did not give a satisfactory response, severe side effects occurred or the therapy was contraindicated [8]. However, there are limited data regarding the usage of biologicals in other subtypes of psoriasis such as erythrodermic psoriasis or GPP [9–11].

Approximately in half of GPP cases treated with biologicals, the tumor necrosis factor (TNF-α) inhibitor infliximab was used. Infliximab similarly to cyclosporine is characterized by the rapid onset of clinical efficacy so it is recommended in the most severe cases [12–14]. In other studies, TNF antagonists such as etanercept and adalimumab were used and recently ustekinumab, an anti-IL-12/23 antibody, was successfully given in recalcitrant GPP [15–18]. Combined therapy, acitretin or methotrexate together with TNF inhibitors, also has been employed [19]. The American National Psoriasis Foundation consensus from the year 2012 on treatment of pustular psoriasis for the first time included infliximab together with acitretin, cyclosporine and methotrexate as the first line options while PUVA, etanercept and adalimumab are considered as second line treatment [3]. Our patient also benefited from infliximab treatment. In reality, two other biologicals (adalimumab and ustekinumab) are available in Poland via treatment programmes reserved for patients with severe (PASI > 18) plaque type psoriasis and psoriatic arthritis, when at least two standard systemic methods have failed or are contraindicated. We will consider these possibilities as the next step.

Biologic therapy seems to bring a benefit in the majority of cases and definitively enriches the therapeutic panel, including patients with uncommon types of psoriasis; however, further studies on larger groups are needed. Many authors have highlighted their safety profile of organ toxicity compared to standard modalities [3], but there are also reports on induction of psoriasis in patients suffering from other immune-mediated diseases such as rheumatoid arthritis or Crohn's disease or exacerbation with pustular flares in psoriatic patients treated with TNF antagonists [20–22]. Some authors believe that these cases are not true psoriasis but rather lichenoid drug reactions in the course of TNF inhibitor therapy [23]. Several newer biologicals such as the anti-TNFs golimumab and certolizumab, the anti-IL-23 MK3222, guselkumab, the anti-IL-17 agents secukinumab, ixekizumab and brodalumab, or small molecules such as apremilast and tofacitinib, are in phase II or III clinical trials and their efficacy may be proved in the near future [24].

CONCLUSIONS

The choice of treatment in GPP should be determined individually and should depend on severity of the disease, age, gender and comorbidities, as well as on the physician's experience with particular methods and their side effects, and finally the availability of therapeutic options should be considered.

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