Drug-related psoriasis

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Psoriasis is a common chronic, systemic immune-mediated, polygenic, and multifactorial skin disorder [1, 2] requiring complex long-term treatment. The onset of psoriasis or relapses of the disease can be caused by various environmental factors including drugs [2] often used to treat comorbidity. Along with classic comorbidities associated with psoriasis such as psoriatic arthritis, inflammatory bowel disease, psychiatric disturbances, and uveitis, there is growing evidence of emerging comorbidities e.g. metabolic syndrome and its components, cardiovascular diseases, non-alcoholic fatty liver disease, chronic kidney disease, etc. [3]. The enlarging spectrum of comorbid disease states in psoriasis patients is associated with the eventual use of a diverse array of medications that may affect the course of psoriatic disease.

Case 1. A 54-year-old male with a 30-year history of psoriasis had typical winter flares of the disease and symptoms of joint pain in the last year. Topical medication consisted of corticosteroids and emollients. Betamethasone sodium phosphate/betamethasone dipropionate IM injection had been administered for his joint complaints before hospitalization. Physical examination revealed indurated scaly plaques, onycholysis, and nail pits. Psoriasis Area Severity Index (PASI) score was 20.4. The patient was overweight (obesity class III) with concomitant arterial hypertension and type 2 diabetes mellitus treated with bisoprolol, lisinopril/amlodipine, aspirin, liraglutide, metformin, gliclazide, and allopurinol. Laboratory data revealed poor glycaemic control with peak blood sugar concentration of 34.4 mmol/l (ref. range 3.75–6.1 mmol/l) and glycosuria. Blood count, creatinine, uric acid and liver function tests were within normal range. Serologic tests for HIV, hepatitis B and C, as well as Quantiferon Gold assay were all negative.

Following consultation with a cardiologist, the β-blocker and angiotensin-converting enzyme (ACE) inhibitor were substituted with verapamil, irbesartan, and indapamide. Treatment of psoriasis included emollients and narrowband UVB (311 nm). Adalimumab was initiated in a standard dose regimen, and PASI 75 at week 16 was achieved.

Case 2. A 53-year-old female with a 2-year history of psoriasis presented with erythematous indurated scaly plaques covering most of the body surface. PASI score was 32.0. Concomitant idiopathic thrombocytopenic purpura had been continuously treated with varying doses of systemic corticosteroids for more than 10 years, the last being oral prednisolone 20 mg daily. Laboratory analysis showed a platelet count of 150 G/l, albumin 34.6 g/l (ref. range 38–51 g/l), and uric acid 370 µmol/l (ref. range 140–340 µmol/l).

Psoriasis was treated with cyanocobalamin 1000 µg, folic acid 0.8 mg t.i.d., cetirizine 10 mg, hydroxyzine 25 mg, and emollients. Oral prednisolone for the concomitant hematologic disorder was not discontinued. At the 2-year follow-up, there was no clinical improvement of psoriasis.

In both cases, psoriasis vulgaris was confirmed by skin biopsy. No clinical or laboratory indicators of infection were detected. The use of systemic glucocorticosteroids, a β-blocker, and an ACE inhibitor was considered a psoriasis exacerbating factor.

In cases of severe, active psoriasis with rapid recurrences or resistance to therapy but also in cases of psoriasis appearing de novo, it is essential to identify plausible precipitating or perpetuating factors such as infections, drugs, stress, etc. [2]. Drugs may exacerbate existing psoriasis or induce psoriasis in patients with or without a family history of psoriasis [4]. In both cases, drug withdrawal may or may not result in remission. The persistence of psoriatic lesions despite discontinuation of the offending drug has been designated as "drug-triggered psoriasis" [4] or "drug-aggravated psoriasis" [5, 6]. At present, the widely accepted general term "drug-induced psoriasis" is commonly used to denote all types of negative effects of drugs on psoriasis irrespective of their nature – induction of psoriasis de novo or exacerbation [7]. In all these possible scenarios, psoriasis may be considered an adverse drug reaction, and the use of the Naranjo probability scale for assessing drug causality of adverse events has been proposed as an addition to the clinical judgment [6, 8]. Depending on the strength of

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the association with psoriasis drugs have been classified into three groups: drugs with an undoubted causal relationship to psoriasis (lithium, β-blockers, antimalarials, etc.), drugs with considerable, but insufficient, supporting data (ACE inhibitors, interferons, etc.) and drugs occasionally reported to be associated with psoriasis (a large group of miscellaneous drugs) [4]. New drug groups including tumor necrosis factor-α (TNF-α) antagonists, immune checkpoint inhibitors have also been reported to be related to psoriasis [5, 6]. Most of the data on the relationship between psoriasis and drugs (except β-blockers, lithium, and TNF-α antagonists) comes from case reports or case series [6] with few case-control and cohort studies available. In 2021, Song *et al.* published the first systematic review and meta-analysis on ACE inhibitor use and psoriasis incidence which established a significant association between this drug group and psoriatic disease [9]. This evidence suggests that 2 major groups of cardiovascular drugs such as β-blockers and ACE inhibitors should be used sparingly, if used at all, in psoriasis patients with comorbidities, and could be implicated as possible culprit drugs in patients with newly developed psoriasis. Confirming drug provocation of psoriasis might be challenging because other triggering factors have to be excluded, and the latency period (time from the start of drug intake and the onset or exacerbation of psoriasis) may be rather too long to suggest any temporal association between the drug and disease.

Systemic glucocorticosteroids are not included in the present guidelines for the treatment of psoriasis although for some of these drugs "psoriasis" is present as an indication in the summary of product characteristics. Potential risks stated in dermatology literature include exacerbation of plaque psoriasis, development of psoriatic erythroderma, and generalized pustular psoriasis, especially after rapid drug discontinuation [1, 5]. Evidence shows that these medications are still largely prescribed not only for managing comorbidities in psoriasis patients but for treating psoriasis itself as well [10, 11]. Systemic glucocorticosteroids are related to "isolated cases" of psoriasis induced or exacerbated by drugs [5]. Because of the discrepancy between the low rates of adverse events in psoriatic patients on systemic glucocorticosteroids and their wide use in this patient population, some argue against the limitation of these agents in psoriasis [10, 12, 13]. Interestingly, a report from the US Food and Drug Administration for the period 2016–2021 determines prednisone as the most common drug related to psoriasis as an adverse event of drug therapy [14]. Systemic glucocorticosteroids have the potential to exacerbate plaque psoriasis and induce severe forms of the disease but these drugs are indispensable in treating certain comorbidities of psoriasis patients. Regarding the overall benefit/risk estimation of drug therapy, the precise drug history, strict clinical monitoring, and the multidisciplinary approach are essential for the proper management of polymorbid patients with psoriasis.

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Conflict of interest

The authors declare no conflict of interest.

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