



## A tale of scale: Corticosteroids and pustular psoriasis

In this issue of the *Journal*, Wong and colleagues<sup>1</sup> describe a severe episode of generalized pustular psoriasis (GPP) in a 69-year-old man with known plaque psoriasis. The episode occurred after repeated courses of systemic corticosteroids for treatment of recalcitrant calcium pyrophosphate arthritis (“pseudogout”).

Recognizing GPP is important, as a high proportion of patients with GPP are systemically ill, and may develop secondary infections with sepsis and multiorgan failure.<sup>2,3</sup> It is often considered a variant of plaque psoriasis—in different series, about 30% to 80% of patients had a history of plaque psoriasis<sup>2</sup>—but it can occur in isolation and has a pathobiology distinct from more routine psoriasis. The pathobiology seems unique, with a dependence on interleukin-36 that is of sufficient magnitude that the interleukin-36 receptor antagonist spesolimab has received regulatory approval specifically for the treatment of GPP flares.<sup>4</sup>

GPP is rare. It seems to be more common in Asian individuals and in women. Subsets of patients have been described with various propensities to recur or have a protracted course. Several case series have described probable precipitants, including infections, pregnancy, external stress, and medications. Best known to internists is the feared association of GPP with withdrawal of corticosteroid therapy prescribed for severe plaque psoriasis or other inflammatory conditions, as presented in this issue by Wong et al.<sup>1</sup>

Digging into the literature on the association of GPP with corticosteroids, given the rarity of this condition, with a few cases per 100,000 patients, it is not surprising to find that there is controversy surrounding the relative need to avoid corticosteroids in patients with psoriasis. Guidelines and textbooks have reinforced concern over the use and withdrawal of corticosteroids in patients with psoriasis, yet strong evidence that defines this association is hard to come by, and corticosteroids seem to be prescribed fairly often.

In 1968, Baker and Ryan<sup>5</sup> described 104 patients with GPP. In approximately one-third of the subset of these patients who had long-standing psoriasis and developed GPP, prior use of corticosteroids was implicated as a trigger for its onset. This and several smaller reports prompted widespread concern regarding corticosteroid treatment for psoriasis. Yet patients with psoriatic arthritis or severe psoriasis, or both, are frequently treated with systemic<sup>6</sup> or intra-articular corticosteroids while waiting for nonsteroid immunosuppressive medications such as methotrexate to take effect or for insurance approval of a newer biologic or targeted biochemical therapy. Gregoire et al<sup>7</sup> in 2021 described 516 patients with preexisting psoriasis who had been treated with systemic corticosteroids and had evaluable follow-up; the calculated flare rate was 1.4%. Attribution of corticosteroids as the cause is difficult, and no flares were described as GPP. One patient had erythroderma

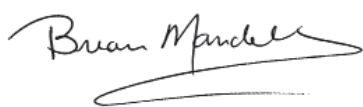
doi:10.3949/cjcm.91b.03024

and responded to a course of corticosteroids. As seen in many of the papers attempting to analyze the relationship between corticosteroids and psoriatic flares, defining a “flare” can be difficult, especially in retrospective studies.

In a systematic review of the literature on psoriatic flares following corticosteroid treatment and withdrawal, Vincken et al<sup>8</sup> selected 21 studies that compared corticosteroid use with no use in patients with psoriasis or psoriatic arthritis. Between 3% and 26% of patients with psoriasis were prescribed corticosteroids in these studies. The 10 observational/interventional studies reviewed did not demonstrate an increase in psoriatic flares of any type after corticosteroid treatment. These included 2 randomized trials comparing the use and non-use of corticosteroids. Notably, the patients in the randomized trials also had received methotrexate or biologic therapy, which may have prevented flares. No information on pustular flares was presented.<sup>8</sup> The authors note in their discussion the metabolic and other risks of corticosteroid therapy, which I think should be highlighted in a patient population already at high risk for the complications from metabolic syndrome. However, the demonstrated benefits of faster disease control gained by adding short-term corticosteroid therapy to methotrexate or other disease-modifying medications should also be noted.

Thus, it seems that corticosteroid use or withdrawal may not be associated with psoriasis flares as often as many of us were taught. Some reported flares with tapering in the older literature may have reflected rebound of incompletely controlled disease on withdrawal of effective therapy, a phenomenon that may occur less often now due to co-administration of effective disease-modifying therapies. Yet we still see descriptions of patients who do have flares,<sup>1</sup> including rare pustular psoriatic flares related to medications. Examples are flares on withdrawal of corticosteroids and the odd but well-recognized occurrence of palmoplantar pustulosis associated with the use of tumor necrosis factor-alpha inhibitors. The perception, and perhaps the reality, that psoriasis flares are occasionally triggered by corticosteroids is reflected in a summary of the US Food and Drug Administration’s Adverse Event Reporting System from 2016 to 2021<sup>9</sup>: prednisone was the leading reported drug for exacerbating or inducing psoriasis, excluding drugs approved to treat psoriasis.

So while caution, careful observation, and patient communication are prudent, the use of corticosteroids to calm severe psoriatic inflammation in skin and joints while awaiting the beneficial effect of a long-term anti-psoriatic medication may have a role in selected patients.



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