



# Ustekinumab-induced remission of recalcitrant guttate psoriasis: A case series

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## INTRODUCTION

Guttate psoriasis is an acute, eruptive form of psoriasis characterized by small, scaly papules and plaques. The exact immunopathogenesis of guttate psoriasis is unclear. However, this subtype of psoriasis shares several features with plaque psoriasis, including an association with group A streptococcal infections and the human leukocyte antigen (HLA)-C\*06:02 allele.<sup>1,2</sup> Although most cases of guttate psoriasis are self-limiting,<sup>3</sup> more severe cases require treatment with topical steroids, phototherapy, or immunosuppressive medications. The use of biologic medications for the treatment of recalcitrant guttate psoriasis has not been systematically studied.

The US Food and Drug Administration has approved ustekinumab, a monoclonal antibody against the shared p40 subunit of interleukin (IL)-12 and IL-23, for the treatment of moderate-to-severe psoriasis, psoriatic arthritis, and Crohn's disease. Its role in the treatment of guttate psoriasis has not been studied. Here we present a series of 6 patients (Table 1) with recalcitrant guttate psoriasis who were treated successfully with ustekinumab, suggesting a potential role for this medication in the treatment of this psoriasis subtype.

## CASE PRESENTATIONS

Patient 1 is a 38-year-old man who with guttate psoriasis that coincided with recurrent streptococcal pharyngitis. Physical examination found scattered, erythematous papules and plaques with scale involving the head, trunk, and extremities. His total

### Abbreviations used:

BSA: body surface area  
HLA: human leukocyte antigen  
IL: interleukin  
PGA: physician global assessment  
Th: T helper

body surface area (BSA) involvement was 20% with an overall Physician Global Assessment (PGA) score of 3. He did not respond to treatment with topical steroids (1 year), oral prednisone (1 week), and cyclosporine (3 mg/kg/d for 2 months). He received a single 90-mg injection of ustekinumab and reported complete clearing of all lesions in less than 4 weeks. He has remained clear for more than 16 months without the need for additional injections.

Patient 2 is a 25-year-old woman with guttate psoriasis that developed after suffering a broken leg. She subsequently experienced recurrent episodes of streptococcal pharyngitis with associated flares of her psoriasis. Skin examination found scattered papules and plaques with scale involving the head and extremities. Her BSA involvement was 5% with an overall PGA score of 2. She did not respond to treatment with multiple courses of oral antibiotics over 2 years, narrowband ultraviolet-B therapy (twice weekly for 2 years), or topical steroids (>2 years). She was treated with ustekinumab, 90-mg injections, at weeks 0 and 8. She noticed improvement shortly after her first injection and was

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**Table 1.** Patient demographics and clinical features

Patient no.	Sex	Age (y)	Guttate psoriasis duration before ustekinumab (mo)	Distribution of lesions	Prior treatments	Ustekinumab dosage (schedule)	Serious adverse effects	No. of injections until clear	Total no. of injections	Length of remission (mo)
1	Male	38	12	Scalp, upper/lower extremities, and trunk	Clobetasol, oral prednisone, cyclosporine	90 mg once	None	1	1	16
2	Female	25	36	Trunk, upper/lower extremities, face, and scalp	Clobetasol, phototherapy	90 mg (weeks 0 and 8), then 45 mg (weeks 23, 35, and 58)	None	2	5	9
3	Male	29	3	Trunk, upper/lower extremities, face, and buttocks	Clobetasol, oral prednisone, cyclosporine	45 mg (weeks 0, 8, 18, and 30)	None	3	4	20
4	Male	26	4	Scalp, axillae, neck, chest, extremities, abdomen, and buttocks	Clobetasol, pimecrolimus cyclosporine	90 mg (weeks 0, 4, then every 8 weeks)	None	2	18	24
5	Female	42	36	Trunk, extremities, and scalp	Phototherapy, cyclosporine	45 mg (weeks 0 and 4)	None	2	2	3
6	Female	35	3	Trunk and extremities	Clobetasol, cyclosporine, apremilast	90 mg (weeks 0 and 4)	None	2	2	7

almost clear at 8 weeks. She was completely clear within 6 months of the first injection and remained clear with 3 additional injections of 45 mg at weeks 23, 35, and 58. She has not required additional injections of ustekinumab and remains clear with only occasional use of topical steroids.

Patient 3 is a 29-year-old man with guttate psoriasis that developed after streptococcal pharyngitis. On examination, the patient had enlarged, erythematous tonsils bilaterally and small erythematous papules coalescing into plaques on his face, trunk, buttocks, and extremities. He did not respond to treatment with topical steroids, oral prednisone, and cyclosporine (5 mg/kg/d for 2 months). He received ustekinumab, 45 mg injections, at weeks 0, 6, 18, and 30. He had complete clearance at the time of his fourth injection and remained clear for more than 20 months until he had another guttate flare after an episode of pharyngitis. He received 2 additional 45-mg injections 4 weeks apart noting significant improvement after a single injection.

Patient 4 is a 26-year-old man on certolizumab pegol for Crohn's disease who had guttate psoriasis after streptococcal pharyngitis. Skin examination found small, erythematous papules and plaques on the trunk, buttocks, and extremities. His BSA involvement was 5% with an overall PGA of 2. He did not respond to treatment with topical steroids, topical pimecrolimus, and cyclosporine (5 mg/kg/d for 4 months). Certolizumab pegol was discontinued, and the patient received ustekinumab, 90-mg injections, at weeks 0 and 6 then every 8 weeks. The patient's BSA decreased from 5% to 1% after the first injection, and his skin was completely clear at the time of his third injection. He has remained clear for more than 2 years and continues receiving ustekinumab injections every 8 weeks for treatment of his Crohn's disease.

Patient 5 is a 42-year-old woman with a 3-year history of mild plaque psoriasis who had a guttate flare after streptococcal pharyngitis. She did not respond to treatment with narrowband ultraviolet B therapy and cyclosporine (4 mg/kg/d for 6 weeks). Skin examination found small erythematous papules and plaques with scale coalescing on her trunk, scalp, and extremities. Her BSA was 40% with an overall PGA of 2. The patient received ustekinumab, 45 mg, at weeks 0 and 4 and was noted to be completely clear at week 12. She maintained clearance for more than 3 months before reverting back to her baseline mild disease.

Patient 6 is a 35-year-old woman on apremilast for chronic plaque psoriasis who had a severe guttate psoriasis flare after streptococcal pharyngitis. Skin examination found well-demarcated erythematous,

scaly plaques located on the trunk and extremities. Her BSA was 10% with an overall PGA of 3. She did not respond to treatment with topical steroids (3 months) and cyclosporine (4 mg/kg/d for 3 months). The patient received ustekinumab, 90 mg, at week 0 and 90 mg ustekinumab at week 4. She was noted to be completely clear at 3 months and has remained clear for 7 months without the need for additional injections.

## DISCUSSION

The treatment of guttate psoriasis includes topical steroids, oral antibiotics, tonsillectomy, cyclosporine, methotrexate, and phototherapy. Multiple studies including a randomized trial suggested a potential benefit of tonsillectomy for guttate or pharyngitis-associated psoriasis, but this finding remains controversial.<sup>4,5</sup> Additionally, a systematic review found no clear evidence supporting the role of oral antibiotics in the treatment of guttate psoriasis.<sup>6</sup> A subset of guttate psoriasis patients do not respond to conventional treatment modalities and represent a challenging patient population.

The pathogenesis of guttate psoriasis is poorly understood. Studies looking at differences in the inflammatory markers (eg, IL-1RA, IL-12p40, IL-17A, IL-22, IL-23, interferon- $\gamma$ , and LL-37/cathelicidin) in psoriasis patients found similarly increased levels in guttate and plaque subtypes compared with those in healthy controls.<sup>7-9</sup> Other studies reported variable results, including a study that showed slightly higher levels of IL-12 and IL-23 in plaque versus guttate psoriasis.<sup>9,10</sup> Overall, these results suggest that the psoriasis phenotypes are not exclusively determined by alterations in inflammatory cytokines, although they may reflect the overall inflammatory burden or disease activity.

Similarly, whether gene variations determine the inflammatory and phenotypic features of guttate psoriasis is also unclear. In an Icelandic patient population, homozygosity for *HLA-C\*06:02* is associated with a 3-fold increased risk of psoriasis, earlier age of onset, and higher likelihood of a positive family history.<sup>11</sup> The high prevalence (83%-100%) of *HLA-C\*06:02* in patients with streptococcal infection-associated guttate psoriasis compared with plaque subtypes is perhaps one of the most compelling arguments for the gene-environment trigger of this disease.<sup>2</sup> Nevertheless, Gudjonsson et al<sup>11</sup> found that *HLA-C\*06:02* homozygosity did not appear to influence the psoriasis phenotype or disease severity. Additionally, not all carriers of the *HLA-C\*06:02* allele or a streptococcal infection go on to have guttate psoriasis, suggesting the presence of unidentified disease mechanisms.<sup>12</sup>

The use of biologic medications, such as ustekinumab, may offer an alternative treatment for patients with chronic or recalcitrant guttate psoriasis. Ustekinumab is a fully human monoclonal antibody that binds the p40 subunit of IL-12 and IL-23, therefore disrupting IL-12R $\beta$ 1 binding and IL-12 and IL-23-mediated cell signaling in T helper (Th) lymphocyte (Th-1 and Th-17) and natural killer cell populations.<sup>13</sup> Despite the elevated levels of IL-12 and IL-23 found in guttate psoriasis patients, ustekinumab's role in this psoriasis subtype has not been formally evaluated. Overall, there is a paucity of randomized controlled clinical trials evaluating the efficacy of interventions commonly used to treat guttate psoriasis.

The use of biologics for guttate psoriasis is not standard of care, as it is commonly self-limited, and biologics are intended for long-term control of chronic plaque psoriasis. However, a phase IIIb trial of patients with chronic plaque psoriasis comparing standard ustekinumab maintenance dosing (45 or 90 mg every 12 weeks) with extended tailored dosing (16, 20, and 24 week intervals) showed that some patients with chronic plaque psoriasis can remain clear/almost clear.<sup>14</sup> It is possible that after induction with ustekinumab, select patients with chronic plaque or chronic guttate psoriasis may obtain disease control with ustekinumab induction or intermittent dosing.

To date, there is only 1 published case report of a chronic guttate psoriasis patient who was successfully treated with ustekinumab.<sup>15</sup> Here we present 6 cases of recalcitrant guttate psoriasis successfully treated with ustekinumab. We acknowledge the limitations of this series, including the small sample size, lack of control group, and variable ustekinumab dosing used. This was not a prospective clinical trial, and we recognize the need for further clinical and laboratory studies to help elucidate the molecular mechanisms driving the pathogenesis of guttate psoriasis. Nevertheless, this limited case series provides strong evidence for the potential benefit of ustekinumab in the treatment of recalcitrant or chronic guttate psoriasis.

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