TNF-α inhibitor–induced psoriasis: A decade of experience at the Cleveland Clinic

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Background: Tumor necrosis factor-α (TNF-α) inhibitor (TNFI)-induced psoriasis remains poorly understood despite having been described 15 years ago. As TNFIs often provide life-changing patient benefits, understanding effective treatments for TNFI-induced psoriasis is important.

Objective: We characterized a cohort of patients with TNFI-induced psoriasis whose psoriasis was specifically diagnosed and managed or comanaged by dermatologists at a single tertiary care institution over a 10-year period.

Methods: Retrospective review of patients in whom TNFI-induced psoriasis was diagnosed between 2003 and 2013.

Results: A total of 102 patients with TNFI-induced psoriasis were identified. The mean age of onset was 40 years, and there was a female predominance (73.5%). Crohn's disease (in 48% of cases) and rheumatoid arthritis (in 24.5% of cases) were the most common primary conditions. Infliximab (in 52% of cases) was the most common inciting agent. The most common TNFI-induced psoriasis subtypes were plaque-type psoriasis (49.5%), scalp psoriasis (47.5%), and palmoplantar pustulosis (41%). Topical medications alone improved or resolved TNFI-induced psoriasis in 63.5% of patients, and cyclosporine and methotrexate (>10 mg weekly) were often effective if topicals failed. Discontinuation of the inciting TNFI with or without other interventions improved or resolved TNFI-induced psoriasis in 67% of refractory cases, whereas switching TNFIs resulted in persistence or recurrence in 64%.

Limitations: Retrospective nature of the study and the fact that some patients may have developed typical psoriasis unresponsive to TNFIs.

Conclusion: Our study cohort represents the largest single-institution cohort of patients with TNFI-induced psoriasis diagnosed and managed or comanaged by dermatologists to date. On the basis of our findings, we propose a treatment algorithm for TNFI-induced psoriasis. (J Am Acad Dermatol 2020;83:1590-8.)

Key words: adverse reaction; drug-induced; palmplantar pustulosis; psoriasiform; psoriasis; TNF-α inhibitor; TNF-α inhibitor–induced psoriasis.

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Tumor necrosis factor-α (TNF-α) inhibitors (TNFIs) have revolutionized management of numerous debilitating chronic inflammatory diseases, including psoriasis vulgaris (PsV), psoriatic arthritis (PsA), rheumatoid arthritis (RA), inflammatory bowel disease (IBD), and ankylosing spondylitis. Like other immunomodulatory medications, TNFIs are associated with mild and potentially serious adverse reactions. One of the most intriguing adverse reactions is occurrence of de novo psoriasiform eruptions. This paradoxic reaction was first reported in 2003, but case reports and series from around the world have made it well recognized.[1,2] Despite the fact that it has been more than 15 years since the first reports of TNFI-induced psoriasis, its pathogenesis, risk factors, prevention, and optimal treatment strategies still remain poorly understood. Here we have characterized a large cohort of patients who were seen at a single tertiary care institution over a 10-year period and developed TNFI-induced psoriasiform reactions (TNFI-induced psoriasis) that were diagnosed and managed or comanaged by dermatologists.

CAPSULE SUMMARY

- Tumor necrosis factor–induced psoriasis is a well-known reaction associated with tumor necrosis factor-α inhibitors, and our 102-patient cohort revealed similarities to other published cohorts.
- Topical medications controlled disease more often than in other cohorts, suggesting that dermatologists should be involved in treating patients with tumor necrosis factor–induced psoriasis. Cyclosporine may represent an underutilized treatment for tumor necrosis factor–induced psoriasis.

MATERIALS AND METHODS

Following institutional review board approval, we searched electronic medical records for patients who, between 2003 and 2013, had been exposed to a TNFI; had seen a dermatologist *after* initiation of treatment with a TNFI; *and* had their condition diagnosed as psoriasis, psoriasiform dermatitis, dermatitis, drug rash, or palmoplantar pustulosis (PPP) after exposure to the TNFI. This search yielded 1448 candidates. One author (S.M.) performed a chart review of all candidates to identify patients who potentially developed TNFI-induced psoriasis. The candidates for inclusion were patients who, during TNFI treatment, (1) developed new-onset psoriasis, (2) developed psoriasis subtype(s) not experienced before, or (3) experienced re-emergence of psoriasis after long-term (>5 years) remission of possible (according to their recollection) psoriasis. Patients must have been evaluated by a dermatologist for the eruption, and the evaluating dermatologists must have described skin lesions consistent with psoriasis and/or expressed the opinion that the eruption was consistent with TNFI-induced psoriasis. Other patients were eliminated.

Potential candidates identified by S.M. were reviewed by another author (A.P.F.) for definitive inclusion or exclusion. Specifically, candidates were further eliminated if the psoriasiform eruption was thought to represent a flare or recurrence of known psoriasis, the eruption was more consistent with an acute adverse drug reaction (morbilliform eruption and/or histologic interface dermatitis), or documentation and/or clinical data were insufficient to confirm TNFI-induced psoriasis. A total of 102 patients met our inclusion and exclusion criteria for a diagnosis of TNFI-induced psoriasis. These patients' charts were then reviewed to extract detailed clinical data.

RESULTS

Of the 102 patients with TNFI-induced psoriasis, 74 (72.5%) were female and 28 (27.5%) were male (F/M ratio, 2.6:1). The mean and median ages at onset of TNFI-induced psoriasis were 40 and 42 years, respectively (range, 8-80 years). The median latency from initiation of the inciting TNFI to onset of TNFI-induced psoriasis was 11 months.

Of the primary conditions for which inciting TNFIs were prescribed, IBD and RA were the most common, accounting for 53 cases (52%) and 25 cases (24.5%), respectively (Table I). Less common primary conditions included PsV with or without PsA (15%) and ankylosing spondylitis (3%). Five patients received TNFIs for other diagnoses. Aside from 15 patients to whom TNFIs had been prescribed for PsV with or without PsA, only 4 additional patients had a history of psoriasis. A family history of psoriasis was noted in 14 of 97 patients (14.4%).

Infliximab was the most common inciting TNFI (in 53 of 102 patients [52%]) (Table I). No patient developed TNFI-induced psoriasis while taking certolizumab or golimumab. In all, 18 patients (18%) were treated with alternative TNFIs before the inciting agent without development of TNFI-induced psoriasis. Additional immunomodulatory agents were taken concomitantly by 64 patients (62.7%) at onset of TNFI-induced psoriasis; these agents included sulfasalazine (n = 4), mesalamine (n = 19), prednisone (n = 11), methotrexate (n = 14), azathioprine (n = 7), hydroxychloroquine (n = 6),

Abbreviations used:

IBD: inflammatory bowel disease
PPP: palmoplantar pustulosis
PsA: psoriatic arthritis
PsV: psoriasis vulgaris
RA: rheumatoid arthritis
TNFI: TNF-α inhibitor

and leflunomide (n = 3). All patients taking hydroxychloroquine had been receiving stable doses for more than 2 years, making it unlikely to play a role in psoriasiform eruptions.[3] The average latency between initiation of an inciting TNFI and onset of TNFI-induced psoriasis was significantly shorter for adalimumab (6 months [range, 3-17 months]) than with infliximab (12.5 months [range, 6-43 months]) and etanercept (13.5 months [range, 5-42 months]) (P = .0187).

Clinical findings

In all, 61 patients (60%) developed more than 1 subtype of psoriasis. Plaque psoriasis was the most common, occurring in 50 of 102 patients (49%), followed by scalp psoriasis (47.5%), PPP (41%), inverse psoriasis (29%), guttate psoriasis (13%), and generalized pustular psoriasis (3%) (Table I). The distribution of psoriasis subtypes varied somewhat depending on the TNFI. Interestingly, the patients who developed TNFI-induced scalp and inverse psoriasis were significantly younger than the patients who developed other subtypes of TNFI-induced psoriasis (Table I).

In all, 27 patients (26.5%) were active smokers at the onset of TNFI-induced psoriasis. Smoking was more likely in patients who developed PPP (43%) than in patients with other psoriasis subtypes (16%). Additionally, smoking was significantly associated with risk of PPP (17 of 27 [62.9%]) but not with risk of other TNFI-induced psoriasis subtypes. Psoriasiform scalp lesions were often associated with significant alopecia.

Biopsy was performed in 43 of 102 patients (42%) to aid diagnosis, whereas the psoriasis of the remaining patients was diagnosed clinically. The primary reaction patterns were spongiotic (n = 6), psoriasiform (n = 28), and psoriasiform plus spongiotic (n = 9). There was no significant difference between the percentage of patients whose eruptions eventually improved and the percentage whose eruptions did not improve on the basis of biopsy-determined primary reaction patterns. Three patients with a psoriasiform reaction pattern had no improvement, whereas all of those with spongiotic or psoriasiform plus spongiotic reaction patterns experienced improvement or resolution. The detailed histologic features in this cohort will be described separately.

Treatment and outcomes

Information concerning treatments and outcomes was available for 100 of 102 patients. Most patients (64%) initially received topical medications (topicals) alone (corticosteroids with or without calcipotriene with or without calcineurin inhibitors). Other treatments, including phototherapy, the addition of or switch to traditional systemic immunomodulatory agents, and/or discontinuation of or switch to another TNFI or biologic, were implemented for cases resistant to topicals alone.

We examined the outcomes of patients to whom various treatment regimens were prescribed while they were continuing to take inciting TNFIs (Table II). Of the 62 patients to whom topicals alone were prescribed, 40 (62.5%) experienced improvement or resolution of their TNFI-induced psoriasis. Methotrexate alone (25 mg/wk) was prescribed for 1 patient with no clinical benefit, whereas methotrexate plus topicals resulted in improvement in 4 of 7 patients (range, 10-20 mg/wk; average, 15 mg/wk) but no benefit in 3 of 7 (range, 7.5-10 mg/wk; average, 8 mg/wk).

Cyclosporine with or without topicals (1.0-3.7 mg/kg) improved or resolved TNFI-induced psoriasis in 5 of 5 patients. Narrowband ultraviolet B plus topicals resulted in improvement or resolution of TNFI-induced psoriasis in 5 of 9 patients. Systemic glucocorticoids with or without topicals resulted in improvement or resolution in 3 of 7 patients. Interestingly, increasing the frequency of TNFIs led to resolution of TNFI-induced psoriasis in 2 patients (1 with PsV and/or PsA [treated with adalimumab] and the other with Crohn's disease [treated with infliximab]).

Next, we examined the outcomes in 25 patients who switched from inciting TNFIs to an alternative TNFI or other biologic after onset of TNFI-induced psoriasis (Table II). Switching TNFIs resulted in persistence or worsening of psoriasis in 16 patients (64%) and improvement or resolution of psoriasis in 9 (36%). In 11 of 25 patients (44%), inciting TNFIs were switched as first-line treatment, whereas the switching of TNFIs in the remaining 14 patients (56%) occurred only after failure of other treatments. In both groups, 64% of patients experienced persistence or worsening of TNFI-induced psoriasis after switching TNFIs. Ustekinumab was prescribed for 4 patients, resulting in improvement or resolution in 3. Four patients were switched to abatacept, resulting in improvement or resolution of TNFI-induced

Table I. Clinical characteristics of patients who developed TNF-α inhibitor–induced psoriasis

Primary diagnoses prompting TNF-α inhibitor treatment in patients who developed TNF-α inhibitor–induced psoriasis		
Primary condition	**Female, n**	**Male, n**
Inflammatory bowel disease	36	17
Rheumatoid arthritis	22	3
Psoriasis with or without psoriatic arthritis	10	5
Ankylosing spondylitis	1	2
Other*	5	1
Totals	74	28

TNF-α inhibitor associated with onset of TNF-α inhibitor–induced psoriasis	
Agent	**Cases, n (%)**
Infliximab	53 (52)
Adalimumab	31 (30)
Etanercept	18 (18)
Certolizumab	0
Golimumab	0

TNF-α inhibitor–induced psoriasis subtypes						
Inciting TNF agent	**Plaque, n (%)**	**PPP, n (%)**	**Pustular, n (%)**	**Scalp, n (%)**	**Inverse, n (%)**	**Guttate, n (%)**
Infliximab	27 (26.5%)	18 (18%)	1 (1%)	31 (30.4%)	21 (20.6%)	5 (5%)
Adalimumab	14 (14%)	14 (14%)	1 (1.9%)	11 (11%)	6 (6%)	5 (5%)
Etanercept	9 (9%)	9 (9%)	0	6 (6%)	2 (2%)	3 (3%)
Totals	50 (49%)	41 (41%)	2 (3%)	48 (47.5%)	29 (29%)	13 (13%)

TNF-α inhibitor–induced psoriasis and age of onset		
Subtype	**Age of onset (median, 25%-75%)**	***P* value†**
Plaque	36.5 (21.3-36.5)	.3475
PPP	44.5 (28.8-60)	.1473
Guttate	52 (42-62)	.0709
Inverse	24 (14-47.5)	.0030
Scalp	29 (16-50)	.0087

PPP, Palmoplantar pustulosis; *TNF*, tumor necrosis factor; *TNF-α*, tumor necrosis factor-α.
*Includes Behçet disease, undetermined inflammatory bowel disease, chronic urticarial vasculitis, juvenile idiopathic arthritis, hidradenitis suppurativa, and Takayasu arteritis.
†Mann-Whitney U test, compared with patients without that subtype.

psoriasis in 3 and worsening in 1. Administration of inciting or alternative TNFIs was restarted in 11 patients whose inciting TNFI had previously been discontinued for 6 months or more. TNFIi-induced psoriasis recurred or persisted in 7 patients (64%), whereas it improved or did not recur in 4.

In all, administration of inciting TNFIs was discontinued in 33 patients (32%) in an attempt to treat the psoriasiform eruption. In 11 of these 33 patients (33%), the TNFI was discontinued as first-line treatment, whereas 22 of the 33 (67%) had failed other treatments before discontinuation of the TNFI (Table II). Of the 11 patients whose TNFI was discontinued as first-line treatment, 7 (64%) experienced improvement or resolution of their TNFIi-induced psoriasis, whereas 4 (36%) had persistence or worsening. Of the 22 patients whose TNFI was discontinued after other treatment failures, 15 (68%) experienced improvement or resolution of their psoriasis and 7 (32%) experienced persistence. In summary, of the 33 patients whose inciting TNFI was discontinued, 22 (67%) had improvement or resolution of TNFI-induced psoriasis, whereas 11 (33%) had persistence or worsening.

DISCUSSION

We have herein described the largest single-institution, dermatology-focused cohort of patients with TNFI-induced psoriasis reported to date; the cohort was drawn from a decade of clinical experience in our department. Our cohort displays numerous similarities to other reported cohorts, including onset of TNFI-induced psoriasis during treatment with various TNFIs, female predominance, lack of a history of psoriasis in most patients, occurrence within a setting of various primary inflammatory conditions, occurrence despite cotreatment with other immunomodulatory agents,

Table II. Treatments and outcomes of patients with TNF-α inhibitor–induced psoriasis

Treatments and outcomes of patients who continued to take the inciting TNF-α inhibitor		
Medications	**Improvement or resolution, n**	**Persistence, n**
Topicals alone	40	22
Methotrexate with or without topicals*	4	4
Cyclosporine with or without topicals	5	0
Systemic steroids with or without topicals	3	4
Ultraviolet B with other treatments	5	4
Increased dose or frequency (adalimumab, infliximab)	2	0
Totals	59	34
Outcomes after switching from the inciting TNF-α inhibitor to other biologic agents		
Biologic attempted after onset of TNF-α inhibitor–induced psoriasis	**Improvement or resolution, n**	**Persistence, n**
Infliximab	0	0
Adalimumab	7	7
Etanercept	1	5
Certolizumab	1	3
Golimumab	0	1
Totals	9	16
Ustekinumab	3	1
Abatacept	3	1
Totals	6	2
Outcomes after a TNF-α inhibitor was restarted following a ≥6-month hiatus		
TNF-α inhibitor restarted	**No recurrence, n**	**Recurrence, n**
Infliximab	1	0
Adalimumab	1	1
Etanercept	1	3
Certolizumab	1	0
Golimumab	0	0
Totals	4	4
Outcome of TNF-α inhibitor–induced psoriasis in patients who discontinued the inciting TNF-α inhibitor		
Inciting TNF-α inhibitor	**Improvement or resolution after D/C* with or without other medications, n**	**Persistence or worsening after D/C with or without other medications, n**
Infliximab	9	6
Adalimumab	9	2
Etanercept	2	3
Certolizumab	2	0
Golimumab	0	0
Totals	22	11†

D/C, Discontinuation; *TNF-α*, tumor necrosis factor-α.

*Does not include patients concomitantly treated with methotrexate at the onset of TNF-α inhibitor–induced psoriasis.

†Of these patients, 5 (3 taking infliximab, 1 taking adalimumab, and 1 taking etanercept) experienced worsening of their psoriasis after discontinuation of drug treatment.

manifestation as various psoriasis subtypes, and variable outcomes.

The female-to-male ratio (2.6:1) of TNFI-induced psoriasis in our cohort is comparable to the ratios reported in literature reviews and larger case series (~1.38-2.73).[4] It has been suggested that female predominance merely reflects the sex distribution of primary conditions for which TNFIs are prescribed.[4] However, some evidence suggests that female sex may be a true risk factor for TNFI-induced psoriasis. A multivariable Cox regression analysis of 7415 patients with IBD, which affects men and women equally, found that female sex was associated with a significantly higher risk of development TNFI-induced psoriasis when controlling for IBD subtype.[5] In our cohort, a 2:1 female predominance existed even for patients with PsV with or without PsA, which also affects men and women equally.

If female sex is a true risk factor for TNFI-induced psoriasis, possible explanations could include hormonal influences or TNFI dosing–based influences, because women generally receive higher TNFI doses

per kilogram of body weight than men do. In our cohort, 33 of 51 patients (65%) who developed TNFI-induced psoriasis while taking infliximab (weight-based dosing) were women, whereas 27 of the 33 (84%) taking adalimumab and 15 of the 19 (79%) taking etanercept (fixed dosing) were women. Alternatively, females with TNFI-induced psoriasis may simply be more likely to seek care.[6]

The majority of our cases (52%) arose in patients who were taking infliximab, which is the most common offender in nearly all reviews and large case series reported.[4,5,7-15] Trends have also emerged concerning latency between initiation of the TNFI and onset of TNFI-induced psoriasis. Our median latency time (11 months) and longest latency times (103 and 118 months) are comparable to those reported in other studies or reviews (range, 6-14.5 months; longest latency, ~120 months).[16] This latency is much longer than expected for most adverse drug reactions, suggesting that additional triggers, such as infections or other stressors, may be needed for onset.

As in other studies, the patients in our cohort most commonly developed plaque psoriasis, followed by scalp psoriasis and PPP. Although PPP accounts for approximately 20% of sporadic psoriasis cases, the prevalence in our cohort was 41%, which is similar to the prevalence of 30% to 43% in systematic reviews.[12,15] Although prior studies have suggested that smoking is a risk factor for TNFI-induced psoriasis, our data suggest that smoking may be a unique risk factor for PPP but not necessarily for other psoriasis subtypes.[5,17,18] Smoking has also been linked to sporadic PPP, suggesting potential pathophysiologic similarities between TNFI-induced psoriasis and sporadic psoriasis.[19,20]

The high prevalence of IBD may explain why inverse psoriasis, which accounts for 3% to 7% of sporadic psoriasis cases, was present in 29% patients in our cohort.[21] Single-institution cohorts of patients with IBD and reviews have also reported higher proportions of patients with inverse psoriasis (9%-20%).[9,14,17] Alternatively, studies with lower proportions of patients with IBD tend to report lower prevalence of TNFI-induced inverse psoriasis (1.7%-3.6%).[10,11,13-15] This suggests that patients with IBD may have unique genetic and/or immunologic factors predisposing them to development of inverse and/or scalp TNFI-induced psoriasis. Additionally, our finding that significant scalp involvement occurred more often in a younger population is supported by previous studies.[21,22]

A significant portion of our analyses focused on treatment of TNFI-induced psoriasis. Given that TNFIs offer life-changing benefits for many patients with chronic inflammatory diseases, identifying effective treatments for TNFI-induced psoriasis that allow continuation of the inciting TNFI is important. Our and past studies suggest that TNFI-induced psoriasis can have various outcomes, ranging from resolution without intervention to persistence despite discontinuation of the inciting TNFI.[23]

The efficacy of topicals alone in our cohort was better (63.5% of cases improved or resolved) than in previously reported cohorts, in which efficacy ranges from 26% to 48% improvement or resolution.[4,5,9,17,23-27] Given that the disease of our patients was diagnosed and managed or comanaged by dermatologists, this higher success rate may be due to more accurate diagnosis and optimal topical management strategies.

Although the overall small numbers of patients make it difficult to draw definitive conclusions, it is worth noting that addition of cyclosporine resulted in better outcomes (5 of 5 patients [100%] experienced improvement or resolution) than did addition of methotrexate or glucocorticoids (7 of 13 patients [53.8%] experienced improvement or resolution). As the disease of 1 patient to whom cyclosporine was prescribed resolved with low dosing and thus relatively mild additional immunosuppression, the use of cyclosporine in treatment of TNFI-induced psoriasis warrants further investigation. Other studies have shown rapid improvement of TNFI-induced psoriasis with addition of cyclosporine.[28-33]

Additionally, methotrexate appeared useful when doses of at least 15 mg weekly were used (4 of 5 patients improved or experienced resolution) compared with when doses 10 mg or less weekly were used (0 of 3 patients improved). However, methotrexate has shown mixed efficacy in treating TNFI-induced psoriasis in other cohorts, with a recent study revealing that only 1 of 8 patients with IBD plus TNFI-induced psoriasis showed long-term benefits after the addition of methotrexate (6 of 8 patients received 25 mg weekly) while they continued to take TNFIs.[14,29,34]

Switching TNFIs resulted in persistence or recurrence of psoriasis in approximately 50% of our patients, and generally in a high percentage of patients in other cohorts.[7,8,25] The outcomes in our cohort were similar regardless of whether the attempts to treat TNFI-induced psoriasis with other medications occurred before switching TNFIs. Interestingly, switching from other TNFIs to adalimumab appeared to result in better outcomes in our cohort compared with other scenarios, with 7 of 14 patients (50%) experiencing improvement or resolution. Furthermore, in the few patients in whom it was attempted, increasing the dose and/or

frequency of the inciting TNFI resulted in improvement or resolution. The reasons for this are unclear but deserve further study.

Finally, discontinuation of inciting TNFIs resulted in 61% of patients having improvement or resolution, 25% showing no benefits, and 14% experiencing persistence or worsening of their TNFI-induced psoriasis. These results are in line with those in previously reported cohorts, in which the psoriasis of 25% to 89% of patients improved or cleared after discontinuation of the inciting TNFIs, and they suggest that in some cases this reaction may trigger typical psoriasis.[4,7,12,27,34,35]

Several studies have shown benefit of switching to other non-TNFI biologics, in particular, to ustekinumab, when TNFI-induced psoriasis is refractory.[29] In our cohort, TNFI-induced psoriasis resolved in 3 of 4 patients who were switched to ustekinumab and 3 of 4 patients who were switched to abatacept. Overall, our results further support discontinuation of inciting TNFIs with or without switching to other biologic classes as a treatment strategy for patients with significant refractory disease.

Our study has several strengths. Our 102 patients represent the largest single-center, dermatology-focused cohort of patients with TNFI-induced psoriasis to date. Our strict inclusion and exclusion criteria and requirement that all diagnoses be made by dermatologists also minimized the chances of inclusion of patients presenting with eruptions not representing TNFI-induced psoriasis. The study's main limitations include its retrospective nature and the possibility that some patients may have developed typical psoriasis not responsive to TNFIs, though the latter is an inherent limitation of all studies. Because we lack data concerning the total number of TNFI prescriptions in our patient population, we are unsure whether infliximab is associated with the highest risk of precipitating TNFI-induced psoriasis or whether it was just the most often prescribed. Similarly, because we do not know how many patients in our population had IBD and RA, we are unsure whether patients with IBD and RA are at higher risk of developing TNFI-induced psoriasis or whether there were simply more such patients in our population who were taking TNFIs than patients with other diagnoses who were taking TNFIs.

We have proposed a treatment algorithm for TNFI-induced psoriasis based on characterization of our cohort (Fig 1). Management of TNFI-induced psoriasis should balance control of the primary disease with minimization of discomfort from skin symptoms. Whenever possible, administration of inciting TNFIs should be continued if providing

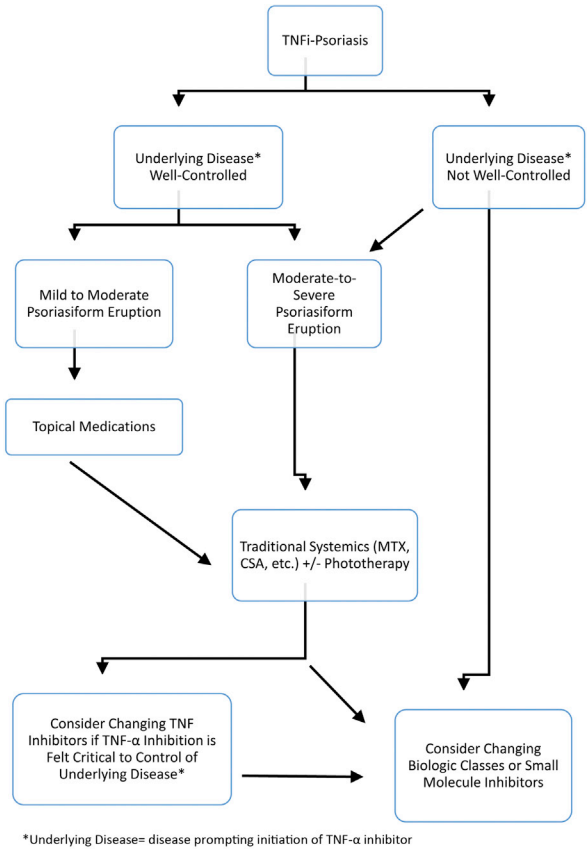

Fig 1. Recommended algorithm for treating tumor necrosis factor-α (TNF-α) inhibitor (TNFI)-induced psoriasis. *CSA*, Cyclosporine A; *MTX*, methotrexate.

significant benefit for primary conditions, especially given the high rates of treatment success with topicals with or without systemic medications, occasional self-limited nature of TNFI-induced psoriasis, and risk of exacerbation of primary conditions if TNFIs are discontinued. For patients with mild-to-moderate disease, we suggest a trial of topicals with or without phototherapy. If it is unsuccessful, the addition of cyclosporine (1-5 mg/kg) or methotrexate (≥10 mg weekly) should be attempted if the potential benefits outweigh the potential risks. If still ineffective, TNFIs should be discontinued in patients with severe TNFI-induced psoriasis or if they are causing significant impairment in the face of less-than-optimal control of primary underlying diseases. In such cases, biologics and/or small molecule inhibitors with alternative mechanisms of action may be beneficial. However, for patients whose underlying disease is well controlled but whose severe TNFI-induced psoriasis is not controlled despite additional systemic medications, it may be reasonable to try transitioning to alternative TNFIs before resorting to medications with alternative

mechanisms of action, given that a subset of patients responds to this strategy favorably.

CONCLUSION

Topicals with or without phototherapy may control TNFI-induced psoriasis in most patients without the need for TNFI discontinuation. When this fails, other strategies may help patients continue taking these agents. Additional studies to better understand this reaction are needed.

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