Tumor necrosis factor-α inhibitor-induced psoriasis: Systematic review of clinical features, histopathological findings, and management experience

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Background: Tumor necrosis factor-α (TNF-α) inhibitors have been reported to induce new-onset psoriasis.

Objective: To better define the demographic, clinical features, and treatment approach of TNF-α inhibitor-induced psoriasis.

Methods: Systematic review of published cases of TNF-α inhibitor-induced psoriasis.

Results: We identified 88 articles with 216 cases of new-onset TNF-α inhibitor-induced psoriasis. The mean age at psoriasis onset was 38.5 years. The most common underlying diseases were Crohn disease (40.7%) and rheumatoid arthritis (37.0%). Patients underwent TNF-α therapy for an average of 14.0 months before psoriasis onset with 69.9% of patients experiencing onset within the first year. The majority of patients received skin-directed therapy, though patients who discontinued TNF therapy had the greatest resolution of symptoms (47.7%) compared with those who switched to a different TNF agent (36.7%) or continued therapy (32.9%).

Limitations: Retrospective review that relies on case reports and series.

Conclusion: While TNF-α inhibitor cessation may result in resolution of induced psoriasis, lesions may persist. Decisions regarding treatment should be weighed against the treatability of TNF-α inhibitor-induced psoriasis, the severity of the background rheumatologic or gastrointestinal disease, and possible loss of efficacy with cessation followed by retreatment. Skin-directed therapy is a reasonable initial strategy except in severe cases. (J Am Acad Dermatol 2017;76:334-41.)

Key words: adalimumab; adverse event; certolizumab; etanercept; golimumab; infliximab; medication side effect; psoriasis; tumor necrosis factor-α-induced psoriasis; tumor necrosis factor-α inhibitor.

The proinflammatory cytokine tumor necrosis factor-α (TNF-α) has been implicated in the pathogenesis of multiple inflammatory and autoimmune conditions such as Crohn disease (CD), ulcerative colitis (UC), rheumatoid arthritis (RA), ankylosing spondylitis (AS), and psoriasis. The development of TNF-α inhibitors has dramatically improved therapeutic options for patients with these conditions. However, there are many reports in the literature of TNF-α inhibitors paradoxically inducing new onset psoriasis or worsening pre-existing quiescent psoriatic disease. A study analyzing the United States Food and Drug Administration Adverse Event Reporting System from 2004-2011 found that TNF-α inhibitors used in the treatment of Crohn Disease were associated with an increased risk of

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psoriasiform adverse events compared to other medications.[1] There is currently no standardized approach for managing TNF-α inhibitor-induced psoriasis, and there is little clarity on whether TNF-α inhibitor therapy should be withdrawn.

The objective of this systematic review of reported cases of TNF-α inhibitor-induced psoriasis was to better define the demographic, clinical, and histological features of TNF-α inhibitor-induced psoriasis and determine the optimal treatment approach.

CAPSULE SUMMARY

- The paradoxical development of psoriasis is an unintended consequence of TNF-α inhibition.
- Discontinuing TNF-α therapy resulted in psoriasis resolution (47.7%) more often than switching (36.7%) or continuing (32.9%) TNF-α therapy.
- TNF-α inhibitor-induced psoriasis is often successfully managed with skin-directed therapies and in many cases does not require cessation of TNF-α—inhibitor treatment.

METHODS

We conducted an electronic literature search to identify studies, case reports, and case series that documented new-onset psoriasiform lesions in patients being treated with a TNF-α inhibitor (Fig 1).

Information sources and search strategy

With the assistance of a research librarian, we identified literature on PubMed on June 18, 2013 using the terms "anti—TNF-alpha", "TNF-alpha inhibitor", "TNF-alpha inhibitors", "TNF-alpha antagonist", "TNF-alpha antagonists", "anti-tumor necrosis factor", "tumor necrosis factor inhibitor", "tumor necrosis factor inhibitors", "tumor necrosis factor antagonist", "tumor necrosis factor antagonists", "infliximab", "adalimumab", "etanercept", "golimumab", "certolizumab", "psoriasis", "psoriasiform"(medical subject headings [MeSH]), "palmoplantar"(MeSH), "pustul*", "induce*", "cause*", "complicat*", "due", "flar*", "exacerbat*", "paradox*", "induct*", "induce*", "advers*", "onset", "associat*", "risk", "non-psoriatic", "psoriasis/chemically induced"(MeSH), "Tumor necrosis factor-alpha/adverse effects"(MeSH). We restricted the search results to English only records. We conducted similar computerized searches using SCOPUS and the Cochrane Database. The last search was conducted on July 1, 2014. Additionally, we reviewed citations within the identified articles and relevant reviews to locate published articles missed by database searches. We used EndNote to identify and remove duplicates.

Study selection

Two investigators (MH and MW) assessed study eligibility using title and abstract for initial screening. Two additional investigators (EW and GB) further evaluated the eligibility of the studies by reviewing the full-text publication. Any study that reported individual data of patients with new-onset psoriasis after the initiation of a TNF-α inhibitor was eligible for inclusion. We excluded records that omitted specific data regarding individual patients, as well as cases in which the patient had a prior history of psoriasis.

Data collection and extraction

Two reviewers (EW and GB) independently extracted individual patient data from each record. We constructed a data collection spreadsheet and extracted the following data items from each record: patient demographics (including age, gender, ethnicity), age at onset of psoriasiform eruption, family history of psoriasis, prior TNF-α inhibitor medication history, disease treatment, TNF-α inhibitor therapy resulting in psoriasiform eruption, time elapsed before onset of psoriasiform eruption, morphology of psoriasiform lesions, body areas involved, biopsy results, recurrence of disease after switching to a different TNF-α inhibitor, concomitant immunomodulator use, concomitant systemic steroid use, management, and response.

RESULTS

Clinical and histopathologic characteristics

Of the 190 full-text articles assessed for eligibility, 88 articles met inclusion criteria for the final analysis. We extracted a total of 216 cases of new-onset TNF-α inhibitor-induced psoriasis from these publications. Demographic features of patients with TNF-α inhibitor-induced psoriasis are summarized in Table I.

Women comprised 72.2% of the cases, with a female predominance in RA and CD (89.9% and 63.2%, respectively). Ages of psoriasis onset ranged from 7 years to 83 years; the mean age of psoriasis onset was 38.5 years. The majority of patients received TNF-α inhibitor therapy for CD (40.7%), followed by RA (37.0%) and AS (13.9%). Patients had a positive family history of psoriasis in 11.8% (N = 19) of disclosed cases (N = 161), and no patients had a personal history of psoriasis or psoriatic arthritis because those cases were excluded from analysis. There were no identified cases with known preexisting psoriatic arthritis before developing psoriasis on TNF-α inhibitor therapy.