The association of psoriasiform rash with anti-tumor necrosis factor (anti-TNF) therapy in inflammatory bowel disease: A single academic center case series

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Dermatologic reactions;
Biologic therapy;
Crohn's enterocolitis;
Ulcerative colitis

Abstract

Background & Aims: Anti-tumor necrosis factors (anti-TNF) including infliximab, adalimumab and certolizumab pegol are used to treat Crohn's disease (CD) and ulcerative colitis (UC). Paradoxically, while also indicated for the treatment of psoriasis, anti-TNF therapy has been associated with development of psoriasiform lesions in IBD patients and can compel discontinuation of therapy. We aim to investigate IBD patient, clinical characteristics, and frequency for the development of and outcomes associated with anti-TNF induced psoriasiform rash.

Methods: We identify IBD patients on anti-TNFs with an onset of a psoriasiform rash. Patient characteristics, duration of anti-TNF, concomitant immunosuppressants, lesion distribution, and outcomes of rash are described.

Results: Of 1004 IBD patients with exposure to anti-TNF therapy, 27 patients (2.7%) developed psoriasiform lesions. Psoriasiform rash cases stratified by biologic use were 1.3% for infliximab, 4.1% for adalimumab, and 6.4% for certolizumab. Average time on treatment (206.3 weeks) and time on treatment until onset of psoriasiform lesions (126.9 weeks) was significantly higher in the infliximab group. The adalimumab group had the highest need for treatment discontinuation (60%). The majority (59.3%) of patients were able to maintain on anti-TNFs despite rash onset. Among patients that required discontinuation (40.7%), the majority experienced improvement with a subsequent anti-TNF (66.7%).
1. Introduction

Anti-tumor necrosis factor (anti-TNF) therapy is used in a variety of autoimmune-mediated diseases and inflammatory conditions, including rheumatoid arthritis (RA), psoriasis, and inflammatory bowel disease (IBD), specifically Crohn's disease (CD) and ulcerative colitis (UC). The complete mechanism of action of these agents is elusive; however their efficacy and safety profile has been proven in the treatment of these conditions.\(^1\) With an increase in the use of anti-TNF agents, including infliximab, adalimumab, and certolizumab pegol, there is also an increased recognition of paradoxical adverse effects, defined as de novo and/or exacerbation of disorders thought to be improved by anti-TNF therapy.

Recent studies have reported the development of new onset cutaneous psoriasis in IBD patients undergoing treatment with anti-TNF agents and the number of cases is increasing.\(^2\)\(^3\) Most of the data on this phenomenon comes from the rheumatology literature; however the association of anti-TNF therapy and dermatologic drug reactions has also had increasing recognition in patients with IBD.\(^4\)\(^5\)\(^6\) Prior studies that have reported this skin phenomenon in IBD patients have concluded that infliximab was associated with the cutaneous reactions in most patients.\(^7\) This evidence is limited in regards to the number of patients exposed to the other anti-TNF agents, adalimumab and certolizumab pegol, as well as the heterogeneity of the studies. Current studies also suggest that this dermatologic phenomenon is a class-effect with all anti-TNF treatments.\(^8\)

The development of anti-TNF induced psoriasiform lesions is of important concern since discontinuation of anti-TNF treatment may impact the patient's underlying inflammatory bowel disease. Any interruption in therapy for side effects thought related to the anti-TNF places the patient at significantly higher risk for development of loss of response to that specific anti-TNF therapy. Therefore, it is critical to understand the natural history and response to therapy of the development of such paradoxical lesions associated with the three anti-TNF therapies.

The aims of this study were to determine the frequency of psoriasiform lesions in an IBD cohort exposed to anti-TNF therapy, the subject characteristics and risk factors associated with the development of psoriasiform lesions in these patients, and to determine the outcome of the skin disease in our single-center academic experience.

2. Materials and methods

2.1. Study design

We conducted a retrospective study for the time period between January 1998 and November 2011 to determine the number of patients with development of new onset or an exacerbation of psoriasiform lesions during treatment with an anti-TNF agent. All patients with a dermatologic reaction were evaluated by a single gastroenterologist and if lesions were severe then referred to a single dermatologist. Psoriasiform lesions were defined as scaly erythematous plaques. Patients with nail involvement, which included nail pitting or discoloration, were also defined as psoriasiform lesions. Histological analysis was not needed for inclusion as the diagnosis of psoriasis is seldom missed given its often classic dermatologic presentation.

Clinical data on all patients with the development of psoriasisform lesions were collected and included age; sex; IBD phenotype; concomitant medication; disease activity at the time of the dermatologic diagnosis based on clinical score instruments (Short Inflammatory Bowel Disease Questionnaire (SIBDQ), Harvey Bradshaw Index (HBI), or the Simple Colitis Disease Activity Index (SCDAI)); and smoking status. A personal or family history of psoriasis, eczema, atopy (which includes atopic dermatitis, asthma, allergic rhinitis and conjunctivitis), or rheumatoid arthritis was also recorded. The extent and distribution of the psoriasiform lesions, dermatological treatments, and histopathology were also reviewed if available. The total time on anti-TNF therapy, time until appearance of dermatologic reaction, time until improvement of the psoriasisform lesion, and impact of anti-TNF discontinuation or switching of treatment on the skin lesion were also recorded.

2.2. Statistical analysis

Data on all cases of psoriasisform lesions were recorded and available for descriptive statistical analysis utilizing STATA SE 11 and R 2.13 software. Stratification was performed based upon treatment with specific anti-TNF agent and included infliximab, adalimumab, and certolizumab pegol. Patients that developed lesions on multiple anti-TNF agents were captured and analyzed as discreet cases. Frequencies of the prevalence of psoriasiform lesions were calculated within each individual stratum and measured against the total number of patients exposed in each anti-TNF group. In addition, outcome variables including: average total time on biologic therapy (anti-TNF); average time on biologic treatment until onset of rash; proportion of patients necessitating topical therapy; proportion of patients with prior anti-TNF exposure history; proportion of patients being treated with concomitant immunosuppressant therapy at the time of onset of rash; proportion of patients requiring discontinuation of anti-TNF therapy due to rash; proportion of patients who required discontinuation of the causative anti-TNF agent and experienced improvement of lesions with subsequent anti-TNF therapy; and all other demographic variables were analyzed for each stratum and reported. The association between the three treatments groups and categorical demographic and clinical characteristic variables was examined by Fisher's exact test.
test among IBD patients with development of a psoriasiform rash; the association between the three treatments and continuous variables was examined by analysis of variance (ANOVA). The significance level was set at $P \leq 0.05$.

2.3. Ethical considerations

The study was approved by the ethics and institutional review board committee of the University of Washington.

3. Results

A total of 1004 patients in our academic center were identified as having exposure to an anti-TNF agent specifically for the treatment of IBD. This included infliximab ($n = 620$), adalimumab ($n = 243$), and certolizumab ($n = 141$). Among 748 patients with Crohn’s disease (CD) and 256 patients with ulcerative colitis (UC), we identified a total of 27 patients with the development of a psoriasiform lesion while receiving an

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic and clinical characteristics of 27 IBD patients with development of a psoriasiform rash.</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Infliximab</td>
</tr>
<tr>
<td></td>
<td>N = 8</td>
</tr>
<tr>
<td></td>
<td>(8/620)</td>
</tr>
<tr>
<td>Demographic characteristics</td>
<td></td>
</tr>
<tr>
<td>Mean age, years</td>
<td>34.6 (SD 9.0)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>6 (75)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>3 (38)</td>
</tr>
<tr>
<td>Previous personal history of psoriasis, n (%)</td>
<td>1 (13)</td>
</tr>
<tr>
<td>Previous personal history of atopy, n (%)</td>
<td>0 (--)</td>
</tr>
<tr>
<td>Family history of psoriasis, n (%)</td>
<td>0 (--)</td>
</tr>
<tr>
<td>Family history of atopy, n (%)</td>
<td>0 (--)</td>
</tr>
<tr>
<td>Family history of arthritis, n (%)</td>
<td>0 (--)</td>
</tr>
<tr>
<td>IBD phenotype</td>
<td></td>
</tr>
<tr>
<td>CD, n (%)</td>
<td>7 (88)</td>
</tr>
<tr>
<td>UC, n (%)</td>
<td>1 (12)</td>
</tr>
<tr>
<td>Age of diagnosis, n (%)</td>
<td></td>
</tr>
<tr>
<td>A1 (below 16 years)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>A2 (between 17 and 40 years)</td>
<td>5 (63)</td>
</tr>
<tr>
<td>A3 (above 40 years)</td>
<td>1 (12)</td>
</tr>
<tr>
<td>Disease location, n (%)</td>
<td></td>
</tr>
<tr>
<td>L1, ileal</td>
<td>1 (13)</td>
</tr>
<tr>
<td>L2, colonic</td>
<td>2 (25)</td>
</tr>
<tr>
<td>L3, ileocolonic</td>
<td>5 (62)</td>
</tr>
<tr>
<td>L4, isolated upper disease</td>
<td>0 (--)</td>
</tr>
<tr>
<td>Disease behavior, n (%)</td>
<td></td>
</tr>
<tr>
<td>B1, non-stricturing and non-penetrating</td>
<td>3 (38)</td>
</tr>
<tr>
<td>B2, strictureing</td>
<td>2 (25)</td>
</tr>
<tr>
<td>B3, penetrating</td>
<td>2 (25)</td>
</tr>
<tr>
<td>NAP, ulcerative colitis</td>
<td>1 (12)</td>
</tr>
<tr>
<td>Disease activity</td>
<td></td>
</tr>
<tr>
<td>Mean SIBDQ</td>
<td>58.7 (SD 7.1)</td>
</tr>
<tr>
<td>Mean HBI or SCDAI</td>
<td>1.86 (SD 1.9)</td>
</tr>
<tr>
<td>Concomitant immunomodulator, n (%)</td>
<td></td>
</tr>
<tr>
<td>Azathioprine</td>
<td>1 (13)</td>
</tr>
<tr>
<td>6MP</td>
<td>0 (--)</td>
</tr>
<tr>
<td>Oral methotrexate</td>
<td>1 (13)</td>
</tr>
<tr>
<td>SQ methotrexate</td>
<td>1 (13)</td>
</tr>
<tr>
<td>NAP</td>
<td>5 (61)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (--)</td>
</tr>
<tr>
<td>Use of immunomodulator at time of rash onset n (%)</td>
<td>3 (38)</td>
</tr>
</tbody>
</table>

a According to Montreal classification.

b Disease activity scoring instruments: SIBDQ, Short Inflammatory Bowel Disease Questionnaire; HBI, Harvey Bradshaw Index; SCDAI, Simple Colitis Disease Activity Index.
Anti-TNF agent between years 1998 and 2011. The prevalence of psoriasiform rash in our IBD patient cohort was 2.1 per 1000 person-years.

Demographics and clinical characteristics of patients are described in Table 1. Overall, psoriasiform lesions were observed in 1.3% (8/620) of patients who received infliximab, 4.1% (10/243) of patients on adalimumab, and 6.4% (9/141) on certolizumab pegol therapy. No lesions occurred during the induction period of the anti-TNF agent or in those patients with high-dose treatment, defined as a dose higher than the standard maintenance therapy. This included patients on infliximab greater than 5 mg per kilogram every 8 weeks, adalimumab 40 mg every 2 weeks or certolizumab pegol 400 mg every 4 weeks.

Among the 27 patients that developed a psoriasiform lesion, the mean age was 39.7 years (SD 10.5) at the time of skin lesion occurrence and the prevalence was female-dominant (70%). Eleven of the patients (41%) were active smokers. A total of 6 patients (22%) had a previous personal history of psoriasis prior to anti-TNF exposure, but no history of atopy. There was no family history of psoriasis, arthritis or atopy among these patients. There were no statistically significant differences in these demographic or clinical characteristic factors among the three treatment groups for the development of a psoriasiform rash.

The majority of psoriasiform lesions occurred in patients with Crohn’s disease (CD) (96%). No statistical difference between CD or UC and the development of a psoriasiform rash was noted.

The mean Short Inflammatory Bowel Disease Questionnaire (SIBDQ) score was 49.4 (SD 11.3) and the highest score was among patients receiving infliximab therapy (58.7, SD 7.1). The lowest Harvey Bradshaw Index (HBI) was also among patients receiving infliximab therapy (1.86, SD 1.9) and the mean HBI score among all patients that developed a psoriasiform lesion was 5.65 (SD 4.8). Clinical disease activity based on SIBDQ (p-value = 0.0054) and HBI (p-value = 0.0117) was statistically different among patients that developed the psoriasiform rash on the three different anti-TNF treatments.

The average time on biologic therapy was 118.8 weeks (SD 85.2). The time between start of anti-TNF therapy until initial appearance of the rash was the longest on infliximab (126.9 weeks, SD 80.5) compared to certolizumab pegol (63.5 weeks, SD 59.5) and adalimumab (40.7 weeks, SD 32.7) (Table 2). Our data showed that there was a significant difference of average time on anti-TNF therapy (p-value = 0.0005) and time between start of anti-TNF until rash appearance (p-value = 0.0157) among IBD patients who developed a psoriasiform rash.

The skin rash was primarily distributed in the predilection sites, which includes scalp, nails, genitalia, extensor surfaces, and the lumbosacral region among all three anti-TNF agents. Palmoplantar pustulosis was the second most common rash distribution.

Among the 27 patients that developed a psoriasiform lesion, therapy was required in 24 of the patients (89%), which included either topical steroid emollient therapy or initiation of thiopurine or methotrexate (Fig. 1). "Favorable response" was defined as greater than 50% of rash improvement following initiation of concomitant rash therapy or the severity of the psoriasiform lesion was mild compared to the potential necessity for discontinuation of anti-TNF therapy. 54% (13/24) of patients were able to maintain on the anti-TNF and eleven patients (46%, 11/24) required discontinuation of the anti-TNF despite concomitant therapy. Among the patients with an unfavorable response to topical therapy or initiation of an immunomodulator, six switched to another anti-TNF agent (55%, 6/11) and 5 patients (45%) required complete discontinuation of anti-TNF therapies due to the severity of their psoriasiform lesions. Of the six patients that were switched to another anti-TNF agent, four of them experienced an improvement in their psoriasiform lesion with the alternate anti-TNF (67%).

Eight patients receiving infliximab developed a psoriasiform rash (1.3%, 8/620) and six required therapy for the rash (75%, 6/8), while two patients had a very mild psoriasiform lesion and no therapy was needed (25%, 2/8). One of these patients ultimately had complete healing of the psoriasiform rash. Only one patient had an unfavorable response despite the addition of topical therapy and concomitant methotrexate, and subsequently required complete discontinuation of anti-TNF therapy (Fig. 2A).

Among a total of 243 patients receiving adalimumab, 10 developed a psoriasiform rash (4.1%, 10/243) and all required initiation of topical therapy and/or initiation of an immunomodulator. 60% required discontinuation of adalimumab (6/10) and four were switched to an alternate anti-TNF agent (67%, 4/6) with a favorable response (Fig. 2B).

### Table 2  Primary characteristics and treatment of psoriasiform rash in 27 IBD patients.

<table>
<thead>
<tr>
<th></th>
<th>Infliximab N = 8</th>
<th>Adalimumab N = 10</th>
<th>Certolizumab N = 9</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average time on anti-TNF therapy weeks (range)</td>
<td>206.3 (SD 95.2)</td>
<td>73.5 (SD 47.6)</td>
<td>91.3 (SD 45.3)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Time between start of anti-TNF until rash appearance, weeks (range)</td>
<td>126.9 (SD 80.5)</td>
<td>40.7 (SD 32.7)</td>
<td>63.5 (SD 59.5)</td>
<td>0.0157</td>
</tr>
<tr>
<td>Primary rash distribution, n (%)</td>
<td>2 (25)</td>
<td>4 (40)</td>
<td>2 (22)</td>
<td>0.7520</td>
</tr>
<tr>
<td>Palmoplantar pustulosis</td>
<td>0 (−)</td>
<td>0 (−)</td>
<td>1 (11)</td>
<td>0.0054</td>
</tr>
<tr>
<td>Flexural sitesa</td>
<td>6 (75)</td>
<td>6 (60)</td>
<td>6 (67)</td>
<td>0.0117</td>
</tr>
<tr>
<td>Predilection sitesb</td>
<td>7 (88)</td>
<td>10 (100)</td>
<td>7 (78)</td>
<td>0.3690</td>
</tr>
<tr>
<td>Topical therapy required n (%)</td>
<td>3 (38)</td>
<td>5 (50)</td>
<td>3 (33)</td>
<td>0.7920</td>
</tr>
<tr>
<td>Discontinuation of current anti-TNF needed n (%)</td>
<td>2 (25)</td>
<td>6 (60)</td>
<td>3 (33)</td>
<td>0.3380</td>
</tr>
</tbody>
</table>

a Flexural or inverse sites include axilla, groin, navel, gluteal cleft and submammary folds.
b Predilection sites include nails, scalp, genitalia, extensor surfaces, and lumbosacral region.
Of 141 patients receiving certolizumab pegol, 9 developed a psoriasiform lesion (6.4%, 9/141) and 8 required initiation of topical steroid therapy and/or an immunomodulator (89%, 8/9), while one patient had a very mild psoriasiform lesion and no therapy was needed (11%, 1/9). This patient ultimately had complete resolution of the psoriasiform lesion. 50% (4/8) required discontinuation of certolizumab pegol and two patients were switched to an alternate biologic agent (50%, 2/4) with ultimate resolution of their psoriasiform lesion (Fig. 2C).

### 4. Discussion

Among a large cohort of anti-TNF treated IBD patients at our single academic center, 27 cases (2.7%) of anti-TNF associated psoriasiform lesions were reported from January 1998 to November 2011. The development of a psoriasiform rash was found in 1.3% of patients that received infliximab, 4.1% with adalimumab and 6.4% with certolizumab pegol. Overall, 60% of patients were able to maintain on their anti-TNF treatment and did not require treatment discontinuation. Two patients (7.4%) had complete healing of the psoriasiform lesions without the need of topical therapy, concomitant agent, or switch to an alternate anti-TNF. Of the cohort of patients who required discontinuation of current anti-TNF therapy, 46% were switched to another anti-TNF and 67% of these patients experienced an improvement in their psoriasiform rash with the subsequent anti-TNF. This suggests that the development of psoriasiform lesions associated with anti-TNF therapies may not necessarily be a class-effect and there may be a pathophysiologic effect due to specific differences in the anti-TNF molecules.
Figure 2  A: Clinical management of infliximab-associated psoriasiform rash in 8 IBD patients. B: Clinical management of adalimumab-associated psoriasiform rash in 10 IBD patients. C: Clinical management of certolizumab pegol-associated psoriasiform rash in 9 IBD patients.
The incidence of psoriasiform lesions associated with anti-TNF therapy has previously been described in the rheumatology literature with a reported incidence rate of 1.04 (95% confidence interval (CI), 0.97–1.54) per 1000 person-years. In IBD patients the incidence rate in a prospective study was described as nearly 5%.9 Recently, Torres et al.6 published a review paper on this phenomenon including 4 retrospective studies, including the results of our current study presented at that time as an abstract, and reported a prevalence range of 1.62–8.8%. In our study, the prevalence of psoriasiform lesions among IBD patients was 2.1 per 1000 person-years. The differences in the incidence in these distinct populations suggest that this paradoxical dermatologic reaction may differ among phenotypically different populations, concomitant therapies for different disorders may affect the frequency of this reaction, and/or there are inherent differences in the molecular composition of each of the anti-TNF treatments and exposure history which contribute to the development of the psoriasiform lesions.

In prior studies, infliximab has been implicated in the majority of the cases of anti-TNF induced psoriasis, including a systematic literature review based on 222 cases of psoriasis (total of 47 studies) in patients with IBD that concluded that infliximab was associated most commonly with the psoriasiform lesions in 69.37% of the patients.7 We propose that this likely reflects the fact that infliximab has been in use longer than the other biologic agents. Additionally, longer-term outcomes related to dermatologic reactions since the availability of the two other anti-TNF agents continue to be limited.

The strength of our retrospective study is the large size of our cohort of IBD patients exposed to anti-TNF therapy and specifically the largest single academic case series to date with the 3 currently available anti-TNF agents compared to previous reports that primarily report on infliximab and adalimumab. Given the significant differences in the construct of certolizumab pegol compared to infliximab and adalimumab, the identification of cases associated with all 3 anti-TNFs adds significant information to our understanding of the pathophysiology and frequency of the development of anti-TNF induced psoriasiform lesions.

None of the patients that developed a psoriasiform rash had a prior history of atopy. This is an interesting observation as approximately 25% of the general population is atopic and these patients have a T helper (Th)-2 phenotype in general.10 Psoirisasis patients have a Th1 phenotype11 and Th1 cytokines have also been implicated in the pathogenesis of inflammatory bowel disease, particularly Crohn’s disease.12 A recent study described that anti-TNF induced psoriasiform skin lesions are characterized by infiltrates of interleukin (IL)-17A/IL-22-expressing Th17 cells and interferon (IFN)-γ-expressing Th1 cells, and the severity of skin disease correlates with the number of IL-17A expressing T cells.9 Thus, Th1 and Th17 cells likely play a major role in the pathogenesis of anti-TNF induced psoriasiform lesions. The authors also have found that anti-IL-12/IL-23 antibody therapy (such as ustekinumab which is currently used to treat psoriasis) is directed against Th1 and Th17 cells, and has a good treatment response to anti-TNF induced psoriasiform lesions. There are ongoing clinical trials investigating the role of ustekinumab at a higher dose in the treatment of CD. It will be interesting at some point to also evaluate its role as a potential alternative in the treatment of IBD patients with anti-TNF induced psoriasiform lesions, as well as to determine the potential risk for the development of

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**Figure 2 (continued).**

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this paradoxical dermatologic reaction among IBD patients exposed to ustekinumab.

There was a significant difference in disease activity based on SIBDQ, HBI, or SCDAI scores among IBD patients who had developed a psoriasiform rash on the three anti-TNFs. Patients on certolizumab had more severe clinical disease activity suggested by the lowest mean SIBDQ score (42.1, SD 9.5; p-value = 0.0054) and the highest HBI/SCDAI mean score (8.44, SD 3.6; p-value = 0.0117) compared to the other two anti-TNF treatment groups. This suggests that those who developed a psoriasiform rash had more clinical disease activity compared to the other anti-TNF treatments. Prior studies have not evaluated the relationship with bowel disease activity and anti-TNF induced psoriasiform skin reactions. Further studies are necessary to evaluate this association, particularly related to Th1 and Th17 cells involved in both skin and gut inflammation.

Patients receiving adalimumab were more likely to require discontinuation of anti-TNF therapy (60%, n = 6/10) compared to patients receiving infliximab (17%, 1/6) and certolizumab (50%, 4/8). Further, the mean duration of time between the start of anti-TNF therapy and appearance of psoriasiform rash was the shortest in patients receiving adalimumab (40.7 weeks, SD 32.7) compared to infliximab (126.9 weeks, SD 80.5) and certolizumab (63.5 weeks, SD 59.5). Our data suggests a significant difference of the time to psoriasiform rash appearance among the three anti-TNF treatments (p-value = 0.0157).

Previous rheumatologic studies have indicated that the risk for new onset psoriasis in patients receiving adalimumab was significantly higher (unadjusted incidence rate 1.84 per 1000 person-years, 95% CI 0.98 to 3.15) compared to infliximab (0.88, 95% CI 0.32 to 1.93) and etanercept (0.59, 95% CI 0.22 to 1.28).8 Although this association is not known in the IBD literature, the GETAID study also observed that the time to onset of psoriasis was shorter among patients receiving adalimumab.5 The fact that our study shows a variable frequency of phenotypes, outcomes, and exposure time to the development among the three anti-TNFs, again suggests that this paradoxical reaction is not a uniform class effect and that the unique physical structure of each molecule likely plays a critical role.

Anti-TNF monoclonal antibodies have been indicated in the creation of an imbalance in the ratio of TNFα and IFNα activity.13,14 We postulate that adalimumab may potentially impact the ratio of TNFα and IFNα activity that is more favorable in the development of psoriasiform lesions compared to the other two monoclonal antibodies, infliximab and certolizumab pegol. This may be because of the differences in the immunochemical composition of adalimumab, which may result in a difference in pharmacodynamic properties that remain poorly understood. The shorter duration in time until onset of psoriasiform rash associated with anti-TNFs administered in the subcutaneous as compared to infusion route may also suggest differences in the molecular characteristics of the anti-TNF agents. Furthermore, a shorter interval in dosing administration of every other week (adalimumab) compared to every 4 weeks (certolizumab pegol) or 8 weeks (infliximab) may play a role in dermatologic outcomes described in our study.

There are some limitations to our study. All cases described are based on a cohort of patients that reported a dermatologic reaction. Therefore, our reported prevalence is an estimate from our retrospective review and not an epidemiological study examining the true incidence. Histologic confirmation was also not necessary for study inclusion and therefore misclassification of dermatologic reaction should also be considered. Secondly, our data is mostly descriptive providing information on clinical and subject characteristics associated with the development of psoriasiform lesions. Our study was not designed to identify predictive factors for the development of psoriasiform rash, as this was a retrospective observational study. As such, our study does not allow risk stratification for the development of psoriasiform lesions prior to the initiation of anti-TNF therapy that would allow physicians to better predict patients at risk. Prior studies have found an association with smoking and higher body mass index as risk factors for the development of psoriasiform lesions.9 Future studies are necessary to evaluate these predictive factors further in a larger exposure cohort of all three anti-TNF agents, including certolizumab pegol and also now with another recent FDA-approved human monoclonal antibody golimumab, as well as the role of anti-IL-12/Il-23 therapies such as ustekinumab.

In conclusion, among a large cohort of anti-TNF treated patients with inflammatory bowel disease in our academic center over a 12-year period, 27 cases of anti-TNF associated psoriasiform lesions are reported. Stratification of these cases by biologic exposure reveals that the discontinuation of anti-TNF treatment is not always necessary. From our academic center experience, initiation of topical steroid emollient therapy was often our first approach in management of the psoriasiform lesion. If the rash persisted or more severe, particularly if there was palmoplantar pustulosis or an inverse psoriasiform rash distribution, then initiation of immunomodulator therapy was considered. If the severity of the psoriasiform lesion was mild compared to the potential necessity for discontinuation of anti-TNF therapy, then from our center experience it may be best to continue dermatologic management with both topical therapy and concomitant agent, as well as maintain the patient on the current anti-TNF. Among those that required discontinuation, dermatologic improvement was achieved in the majority of cases with a subsequent anti-TNF agent, suggesting that the development of psoriasiform lesions is not necessarily a class effect and patients can be switched to another anti-TNF without recurrence in many instances.

Disclosures of conflict of interests

Dr. Afzali is a speaker and consulting physician for UCB and Abbvie. Dr. Lee is a speaker and consulting physician for UCB, Abbvie and Janssen. He also is a principal investigator in the UNITI (ustekinumab) clinical trials. For the remaining authors, none were declared.

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Authors’ contribution

AA conceived the study concept and design, and carried out the acquisition of data, statistical analysis and interpretation...
of data, drafting of manuscript, and critical revision of the
manuscript for important intellectual content. CW performed
the statistical analysis, interpretation of data, and revision of
the manuscript. JKH also performed the statistical analysis
and interpretation of data. JEO carried out critical revision
and approval of final manuscript. SDL conceived the study
concept and design, and performed critical revision and
approval of final manuscript. All authors read and approved
the final manuscript.

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