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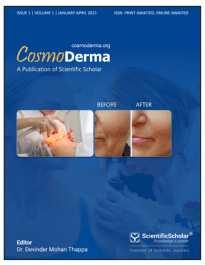

*Case Report*

# Tofacitinib in the treatment of recalcitrant cases of psoriasis vulgaris

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## ABSTRACT

Treatment of recalcitrant cases of psoriasis vulgaris can pose a major challenge to dermatologists. Despite the availability of various drugs and treatment modalities, these cases often either show unsatisfactory response to these treatments or may have to be discontinued due to development of adverse effects or may be contraindicated due to underlying morbidities. After exhausting the conventional modalities such as methotrexate, cyclosporine, acitretin, apremilast, and phototherapy, the next line of management involves usage of biologicals. Biologicals, although efficacious in most cases, come with their own set of drawbacks including cost, availability, and risk of development of anti-drug antibodies, rendering them ineffective. Furthermore, some patients have found to relapse within a few months of stopping them. We present a case series of five patients of refractory psoriasis vulgaris who had exhausted all conventional modalities (including biologicals in three of the patients) who were successfully treated with tofacitinib, a small molecule inhibiting Janus kinase 1/3 enzyme. Our patients have reported no side effects with tofacitinib till date and are continuing to maintain the results. From this series, we conclude that tofacitinib may be an effective therapy for the management of recalcitrant psoriasis.

**Keywords:** Psoriasis, Recalcitrant, Janus Kinase, Tofacitinib

## INTRODUCTION

Psoriasis is a chronic papulosquamous disorder of multifactorial etiology. The disease has a relapsing and remitting course with no cure till date. There are many treatment modalities available including methotrexate, cyclosporine, acitretin, apremilast, and phototherapy. However, each of these are associated with side effects. Methotrexate is an inexpensive and popular immunosuppressant but has the risk of mucositis, pneumonitis, pancytopenia, and cutaneous ulceration due to acute toxicity with dose-dependent or idiosyncratic mechanisms.[1,2] Cyclosporine can result in hypertension, renal toxicity and it is recommended to keep the duration of its use below 2 years.[3] Acitretin can cause hyperlipidemia, hepatotoxicity, and its prolonged teratogenic potential limits its use in women of child bearing age group. Phototherapy facility is not available at all setups and patients may be unable to make multiple hospital visits each week for it.

Biologics are expensive and development of anti-drug antibodies can render even these expensive drugs ineffective. Hence, in patients who have exhausted these modalities, the treatment options are limited. We successfully treated five such cases with tofacitinib.

## CASE REPORTS

Patient 1 was a 70-year-old male with chronic plaque psoriasis since 18 years. He was on methotrexate for more than 5 years with cumulative dose exceeding 3 grams. His liver function tests were deranged. Acoustic radiation force impulse imaging, used as a measure for liver fibrosis, was suggestive of severe liver scarring. The patient had received phototherapy for over 2 years with no improvement. The patient developed severe diarrhea with apremilast and cyclosporine had to be discontinued due to development of hypertension and rising creatinine values. Despite these treatments, his Psoriasis Area and Severity Index (PASI) was 19.5 with around 60% involvement of body surface area (BSA) [Figure 1a]. After performing the required baseline investigations, the patient was started on tablet tofacitinib 5 mg once a day after getting a clearance from gastroenterology. Within 2 months of treatment, PASI 75 was achieved with <10% BSA involvement [Figure 1b].

Patient 2 was a 42-year-old male with psoriasis since 20 years with history of joint pain and swelling. He was treated with methotrexate on and off for 10 years with cumulative dose exceeding 4 g but was stopped due to deranging liver function and episodes of malena. Ultrasonography of abdomen showed hepatomegaly and altered liver echotexture and liver biopsy was suggestive of methotrexate induced liver injury. The patient also received cyclosporine on and off for a duration of 3 years but developed nephrotoxicity. A renal biopsy suggested focal segmental glomerulosclerosis, 20% interstitial fibrosis and tubal atrophy. He also developed a rarely reported side effect of cyclosporine – sensorineural hearing loss.[4] The patient was unable to make multiple hospital visits for phototherapy and developed severe diarrhea with apremilast. At the time of presentation to our hospital, the patient had PASI of 26.2 and BSA involvement of more than 60%. He was found to be positive for hepatitis C virus (HCV) antibody, but HCV ribonucleic acid was undetectable. After performing the required investigative workup and obtaining clearance from gastroenterology, the patient was started on injection secukinumab. A total of five loading doses of 300 mg each were given at weekly intervals and the patient showed complete lesion clearance. Following this, he was started on monthly maintenance doses which, however due to limited supply, were discontinued. The patient flared within 3 months of stopping the injections and PASI increased to 14.2 and BSA involvement was 40%.

The patient was started on tofacitinib 5 mg twice a day and, within 1 month, PASI 75 was obtained. The BSA involvement reduced to <10% and PASI reduced to 3.3.

Patient 3 was a 41-year-old man with psoriasis vulgaris since 10 years. The patient showed no improvement with 15 mg weekly dose of methotrexate. He showed some improvement with cyclosporine which was given for 1 year but lesions flared as soon as the dose was tapered and the drug was stopped. The patient did not tolerate apremilast due to troublesome diarrhea. Phototherapy too showed no improvement. His lesions improved with injection secukinumab, but his maintenance therapy was interrupted due to the COVID-19 pandemic. At his subsequent visit to the hospital, his PASI was 32 and around 70% of BSA was involved [Figure 2a]. The patient was worked up and started on tablet tofacitinib 5 mg twice daily and, within 3 months, PASI 75 was achieved and BSA involved reduced to 15% [Figure 2b].

Patient 4 was a 52-year-old man, a known case of chronic kidney disease with psoriasis vulgaris since 20 years. He was on methotrexate on and off for around 15 years with no improvement. Due to his renal condition, usage of

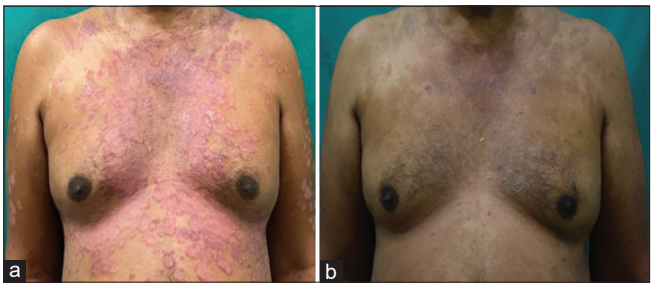


**Figure 1:** (a) Pre-tofacitinib photo of patient 1. (b) Post-tofacitinib photo of patient 1.

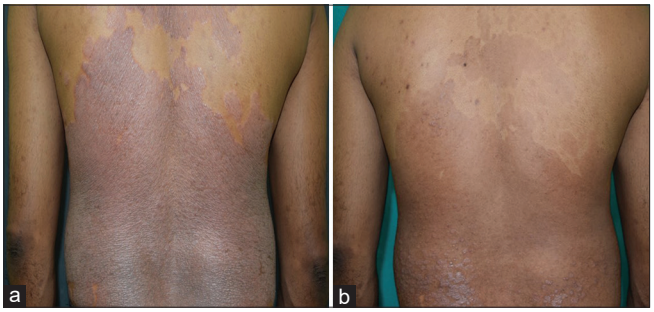


**Figure 2:** (a) Pre-tofacitinib photo of patient 3. (b) Post-tofacitinib photo of patient 3.

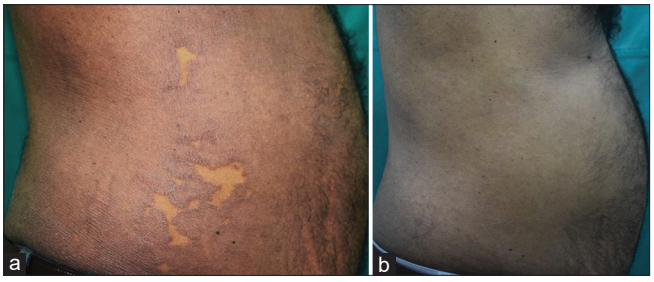


**Figure 3:** (a) Pre-tofacitinib photo of patient 5. (b) Post-tofacitinib photo of patient 5.

**Table 1:** Details of patients treated with tofacitinib.

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 |
|---|---|---|---|---|---|
| Age (years) and sex | 70<br>Male | 42<br>Male | 41<br>Male | 52<br>Male | 43<br>Male |
| Duration of psoriasis (years) | 18 | 20 | 10 | 20 | 15 |
| Co-morbidities | Delusional disorder | Anti HCV positive, depression | Nil | Chronic kidney disease, diabetes mellitus, hypertension | Nil |
| Treatment history | 1. Methotrexate:<br>• Derangement in liver function<br>• Caused severe liver scarring<br>2. Phototherapy:<br>• No improvement<br>3. Apremilast:<br>• Caused severe diarrhea<br>4. Cyclosporine:<br>• Caused hypertension and rising creatinine levels | 1. Methotrexate:<br>• Deranged liver function<br>• Developed malena<br>2. Cyclosporine:<br>• Developed focal segmental glomerulosclerosis and interstitial fibrosis and tubular atrophy<br>• Developed bilateral sensorineural hearing loss<br>3. Apremilast:<br>• Developed troublesome diarrhea<br>4. Secukinumab:<br>• Flared on stopping | 1. Methotrexate:<br>• No improvement<br>2. Cyclosporine:<br>• Lesions flared as soon as tapered<br>3. Apremilast:<br>• Caused troublesome diarrhea<br>4. Secukinumab:<br>• Initial improvement but was unable to follow up due to COVID-19 pandemic | 1. Methotrexate:<br>• Used for 15 years with no improvement<br>2. Apremilast:<br>• No significant improvement | 1. Methotrexate:<br>• No improvement<br>2. Cyclosporine:<br>• Flared on tapering<br>3. Apremilast:<br>• No improvement<br>4. Secukinumab:<br>• Initial improvement but flared within 1 month of stopping |
| Dosage of Tofacitinib | 5 mg once daily | 5 mg twice daily | 5 mg twice daily | 5 mg once daily | 5 mg twice daily |
| PASI Score before starting Tofacitinib | 19.5 | 14.2 | 32 | 19.9 | 22.9 |
| PASI score at present | 4.8 | 3.3 | 6.4 | 2.4 | 2.1 |
| BSA involvement before starting Tofacitinib | >60% | 40% | >70% | 35% | >70% |
| BSA involvement at present | <10% | 10% | <15% | <5% | <5% |
| Duration in which PASI 75 was achieved | 2 months | 1 month | 3 months | - | - |
| Duration in which PASI 90 was achieved | - | - | - | 2 months | 1 month |
| Tofacitinib therapy ongoing | Yes | Yes | Yes | Yes | Yes |
| Duration (in months) for which Tofacitinib has been given till date | 11 | 10 | 10 | 8 | 6 |
| Adverse effects | None noted | None noted | None noted | None noted | None noted |

BSA: Body surface area, HCV: Hepatitis C virus, PASI: Psoriasis area and severity index

cyclosporine was restricted. Apremilast did not show any significant improvement. The patient was worked up for tofacitinib and clearance was obtained to start it at 5 mg once daily dosing only. His baseline PASI score was 19.9. He was started on tofacitinib 5 mg once daily dose and, within 2 months, his lesions showed near complete clearance. His PASI reduced to 2.4 by 3 months.

Our 5th patient was 43-year-old man with psoriasis since 15 years with episode of erythroderma and hospital admission 7 years back. He was treated with multiple courses of cyclosporine and flared each time it was tapered. Methotrexate was given for 3 years with no improvement. Apremilast too showed no improvement. Next, the patient was worked up and started on injection secukinumab. Although he showed significant improvement with secukinumab, the lesions flared within 1 month of stopping. At the time, the patient was being worked up for tofacitinib that his PASI was 22.9 with BSA involvement of about 70% [Figure 3a]. Within just 1 month of starting tofacitinib 5 mg twice daily, PASI reduced to a mere 2.1 and BSA involvement reduced to 5%. Thus, PASI 90 was achieved in just 1 month [Figure 3b].

## DISCUSSION

We present five cases of psoriasis who were refractory to various systemic therapies [Table 1]. In all patients, oral tofacitinib resulted in significant improvement with PASI 75 being achieved as early as 1 month (patient 2) and PASI 90 being achieved as early as 1 month (patient 5). All our patients are maintaining the results achieved with tofacitinib till date and no side effects have been noted.

Tofacitinib is a small molecule which inhibits Janus associated kinase 1 and 3. It is Food and Drug Administration (FDA) approved for rheumatoid arthritis, psoriatic arthritis, ulcerative colitis and juvenile idiopathic arthritis above 2 years of age.[5] The off label uses in dermatology include alopecia areata, atopic dermatitis, psoriasis vulgaris, vitiligo, dermatomyositis, lichen planopilaris, pyoderma gangrenosum, and morphea.[6]

Psoriatic skin shows upregulated Janus kinase (JAK)/signal transducers and activators of transcription signaling as compared to healthy skin, causing the production of multiple proinflammatory cytokines such as interferon-gamma, interleukin (IL)-12, and IL-23.

Inhibition of JAK signaling therefore has an overall anti-inflammatory effect, with decreased expression of proinflammatory cytokines.[7-9]

Various adverse effects have been reported with tofacitinib use including infections, malignancies, deep vein thrombosis, and hyperlipidemia. As per FDA recommendations, before starting the drug one must check for latent tuberculosis especially in a country like India the tests which should be done before starting medications and periodically include complete blood count, lipid level and liver function tests.[10]

## CONCLUSION

Although previous studies have demonstrated the efficacy of tofacitinib in moderate to severe large plaque psoriasis, our case series shows its efficacy in difficult cases of psoriasis where patients are refractory to conventional modalities of treatment. Hence, we conclude that tofacitinib may be an effective therapy for the management of recalcitrant psoriasis.

### Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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