



TARGETED RESCUE THERAPY IN REFRACTORY ULCERATIVE PROCTITIS: A CASE REPORT ON TACROLIMUS ENEMA

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ABSTRACT

Background: Ulcerative proctitis, a localized subtype of ulcerative colitis (UC), is generally managed with mesalamine therapies. However, some patients fail to respond and require alternative strategies. Among emerging treatments, topical tacrolimus offers potent localized immunosuppressive effects with minimal systemic exposure. **Case Presentation:** We present a case involving a 37-year-old woman with a 10-year history of ulcerative proctitis who experienced a flare-up with rectal bleeding and increased stool frequency. Her symptoms did not improve despite optimized oral and rectal mesalamine therapy and a short course of antibiotics. The baseline Mayo score was 10, and the UCEIS score was 7, both indicating severe disease activity. Sigmoidoscopy showed grade 3 proctitis, with signs of active inflammation. The patient was started on a once-daily tacrolimus enema (4mg/60 mL) while continuing oral mesalamine. Within 10 days, her symptoms improved significantly; bowel movements normalized, and bleeding resolved. A follow-up sigmoidoscopy revealed near-complete mucosal healing, now consistent with grade 1 proctitis. No adverse effects were observed during treatment. **Conclusion:** Tacrolimus enema is a safe and effective option for treating refractory ulcerative proctitis. Early intervention may promote rapid remission and reduce the need for systemic corticosteroids.

KEYWORDS : Ulcerative proctitis, tacrolimus enema, mesalamine-refractory, calcineurin inhibitor, mucosal healing, inflammatory bowel disease

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory condition of the colon that typically follows a relapsing-remitting course. Among its various forms, ulcerative proctitis (classified as E1) is the most localized, with inflammation limited to the rectum. Standard treatment for this type of disease usually involves mesalamine (5-aminosalicylic acid [5-ASA]), administered both orally and rectally. Although most patients respond well to 5-ASA therapy, an estimated 15–20% may not achieve remission and require more intensive treatment [1].

In such refractory cases, clinicians often consider topical or systemic corticosteroids, immunomodulators, or biologics. However, systemic therapies can pose risks, particularly when treating patients with localized disease and minimal systemic symptoms. Tacrolimus, a calcineurin inhibitor that suppresses T-cell activity, has emerged as a potential alternative. When delivered topically through enemas or suppositories, it achieves high drug levels at the site of inflammation while minimizing systemic absorption—making it especially appealing for distal forms of UC, including proctitis [2].

Recently, a lipid-based tacrolimus enema (4mg/60ml) has been approved in India for achieving clinical remission in patients of mild to moderate left-sided colitis (including proctitis and proctosigmoiditis) refractory to mesalamine therapy. Studies have shown promising results for rectal tacrolimus in steroid-refractory distal UC. A case series has documented rapid symptom relief and mucosal healing, allowing patients to avoid systemic drugs or even surgery [3,4]. Despite this encouraging data, real-world evidence remains scarce, particularly in patients who are refractory to mesalamine but have not yet received steroids.

In this case report, we describe a young woman with a long-standing history of ulcerative proctitis, which had been stable with mesalamine therapy until she developed an acute flare. Her symptoms did not improve with intensified 5-ASA treatment, but she responded quickly and effectively to tacrolimus enema, achieving clinical and endoscopic remission without needing systemic steroids or other immunosuppressants.

Case Presentation

A 37-year-old woman, previously diagnosed with ulcerative colitis since 2013, specifically the E1 type (ulcerative proctitis), came to the outpatient department with a five-day history of worsening lower gastrointestinal symptoms. She noted a significant increase in stool frequency (about 6–7 times daily), along with visible rectal bleeding and mucous discharge. She had no fever, abdominal discomfort, weight loss, or symptoms outside the gastrointestinal tract. There were no signs of systemic involvement.

Her condition had remained well-controlled for nearly ten years on maintenance oral mesalamine (2.4 g/day), occasionally supplemented

with mesalamine enemas. She had never required systemic corticosteroids, immunomodulators like azathioprine, or biologics. She had no relevant comorbidities or family history of inflammatory bowel disease or colorectal cancer.

Five days before her visit, she had begun with a 5-day course of ofloxacin 200 mg plus ornidazole 500 mg combination, administered twice daily, prescribed at another clinic, suspecting an infection. However, her symptoms persisted. She did not have any history of recent travel, change in diet, or eating questionable food. There was no recent NSAID use, risky sexual behaviour, or prior pelvic radiation exposure.

On physical examination, she appeared clinically stable and afebrile, with typical vital signs. Abdominal examination was unremarkable—there was no tenderness, bloating, or organ enlargement. The perianal area showed no abnormalities such as fistulas or skin tags.

Initial laboratory analysis revealed a haemoglobin level of 12.6 g/dL, a slightly raised C-reactive protein (CRP) of 4.2 mg/L, and an ESR of 26 mm/hour—suggesting mild inflammation. Stool cultures ruled out common enteric infections, including *Salmonella*, *Shigella*, *Campylobacter*, and *Clostridium difficile*. Cytomegalovirus (CMV) PCR was also negative. Stool calprotectin testing was not conducted.

Flexible sigmoidoscopy showed grade 3 proctitis with pronounced mucosal erythema, friability, erosions, and spontaneous bleeding limited to the rectum (Figure 1A). The baseline Mayo score was 10, and the UCEIS score was 7, both indicating severe disease activity. There were no skip lesions or signs of inflammation in other proximal areas of the colon.

Management Approach:

Given her localized disease, poor response to optimized mesalamine therapy, and reluctance to start systemic steroids, a steroid-sparing approach was chosen. She was started on a once-daily tacrolimus enema (4mg/60mL) while continuing the same dose of oral mesalamine. Her previous dose of oral mesalamine (4.8 g/day) was continued concurrently during the 10-day tacrolimus therapy. Supportive care included dietary adjustments, hydration, and scheduled follow-ups. Detailed instructions on enema use and potential side effects were provided.

Clinical Response:

By Day 10, her Mayo score had reduced to 3, indicating a substantial improvement. Her bowel movements had normalized to 1–2 formed stools per day, and rectal bleeding had subsided entirely. She experienced no urgency, tenesmus, or abdominal discomfort. Additionally, she did not report any side effects or local irritation.

A follow-up sigmoidoscopy on Day 10 revealed substantial mucosal

healing, consistent with grade 1 proctitis. Only minimal erythema was observed, with no evidence of bleeding or erosions (Figure 1B). The patient expressed satisfaction with her progress.

After achieving remission, tacrolimus enema was tapered to alternate-day administration for 20 days while continuing oral mesalamine at 4.8 g/day. Subsequently, the tacrolimus was discontinued, and she remained on mesalamine monotherapy.

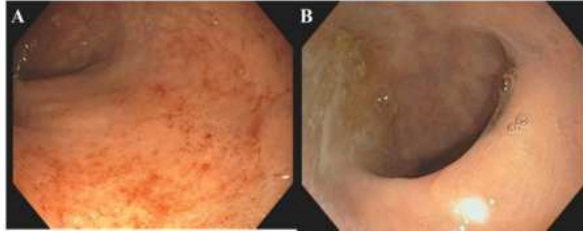


Figure 1: Sigmoidoscopy findings. A: Baseline sigmoidoscopy showing grade 3 proctitis. Marked mucosal erythema, friability, erosions, and spontaneous bleeding are evident, consistent with active moderate to severe inflammation. B: Follow-up sigmoidoscopy on Day 10 post-tacrolimus enema therapy. Significant mucosal healing is seen, with only minimal erythema, absence of active bleeding or erosions, consistent with grade 1 proctitis.

DISCUSSION

Ulcerative proctitis is a localized form of ulcerative colitis limited to the rectum and is usually treated effectively with oral and rectal formulations of mesalamine. While many patients respond well to this standard approach, a small proportion remains unresponsive, requiring escalation to more potent immunosuppressive or biologic therapies. However, in cases with limited disease extent, using systemic medications can pose potential risks, making targeted local treatments a safer alternative.

Tacrolimus, a calcineurin inhibitor, works by blocking T-cell activation and reducing the production of inflammatory cytokines like interleukin-2. Although it is more commonly used systemically for patients with steroid-refractory UC, rectal formulations such as enemas or suppositories have gained attention for treating distal colitis and proctitis [1]. This delivery method allows for high local drug levels at the site of inflammation with minimal systemic absorption, reducing the potential for systemic toxicity.

In the current case, the patient had been in remission for nearly 10 years on oral mesalamine but developed an acute flare that did not improve with intensified mesalamine therapy or antibiotics. Given the lack of response and her preference to avoid systemic steroids, she was started on tacrolimus enema. Remarkably, within 10 days, she showed both clinical and endoscopic remission, and she experienced no side effects. This aligns well with existing literature supporting the effectiveness of rectal tacrolimus in similar scenarios.

For example, Uchino et al. demonstrated that rectal tacrolimus enema produced clinical improvement in 90% of patients with antibiotic-refractory pouchitis [4]. Likewise, Panés et al. found that 68.4% of patients with distal UC improved after four weeks of rectal tacrolimus therapy at doses between 2 and 4 mg/day [5]. A systematic review also reported clinical response rates of up to 96% and mucosal healing in 40–50% of cases treated with topical tacrolimus for steroid-refractory UC [1].

Several studies have explored the role of rectal tacrolimus in managing proctitis that does not respond to standard therapies. Van Dieren and colleagues [6] treated 19 patients—7 with distal colitis and 12 with ulcerative proctitis—using either enemas or suppositories containing 2–4 mg of tacrolimus daily for four weeks. The treatment was well tolerated, with no reported adverse effects or signs of systemic drug absorption. Most patients with ulcerative proctitis showed meaningful symptom relief, and those receiving suppositories had notable improvement on histology, pointing to the potential benefit of locally applied tacrolimus in such cases.

Similarly, Lawrance and Copeland [7] conducted a pilot study using a topical tacrolimus ointment (0.3 mg/mL, 3 mL twice daily) in patients with resistant ulcerative proctitis. All participants had previously failed conventional treatments. After eight weeks, six out of eight

patients achieved remission, and several were able to taper off steroids. The therapy was well tolerated, with no significant side effects reported, further supporting its possible role in difficult-to-manage proctitis.

In another study, Fehily and colleagues [8] assessed a more practical approach by preparing tacrolimus enemas using tap water and the contents of 1 mg capsules. Seventeen patients—mostly with long-standing, treatment-resistant UC or CD—were treated with daily enemas and later shifted to a maintenance schedule. Over 60% of UC patients achieved endoscopic remission, with improvements in rectal bleeding, stool frequency, and inflammatory markers. The treatment was safe, easy to prepare, and well tolerated, making it a promising alternative for those with refractory proctitis.

Together, these studies demonstrate growing evidence that rectally administered tacrolimus, whether as ointments, suppositories, or simple enemas, can offer a safe and effective option for managing treatment-resistant proctitis.

Moreover, findings from Miyoshi et al. showed that patients who achieved mucosal healing with oral tacrolimus had significantly better outcomes over two years, as measured by the Mayo endoscopic score [9]. Although our patient received tacrolimus rectally, her rapid mucosal healing may indicate a similarly favorable long-term prognosis.

One of the key concerns with systemic tacrolimus therapy is safety. Systemic administration has been associated with adverse effects such as nephrotoxicity, neurotoxicity, and infections. However, when used rectally, these risks appear to be significantly lower. In the current case, the patient tolerated the enema well and reported no adverse events, suggesting that topical delivery can be a safer option. That said, there's still a need for more robust long-term safety data for rectal tacrolimus.

This case emphasizes the potential role of tacrolimus enema as a second-line treatment for patients with mesalamine-refractory ulcerative proctitis. When used early in well-chosen patients, it may help achieve both symptom relief and mucosal healing while avoiding the need for systemic immunosuppression.

CONCLUSION

This case highlights the successful use of topical tacrolimus enema as a rescue therapy for a patient with mesalamine-refractory ulcerative proctitis. The treatment led to rapid clinical improvement and mucosal healing without the need for systemic corticosteroids or the emergence of any side effects. Tacrolimus enema offers a promising alternative for patients with distal ulcerative colitis who do not respond to mesalamine, particularly when alternative systemic therapies or steroids are to be avoided. However, more prospective research is needed to assess long-term outcomes and better define its place in the treatment landscape of distal UC.

Patient Consent:

Informed consent was obtained from the patient for publication of this case report and accompanying images.

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