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CASE REPORT

A case of refractory chronic pouchitis successfully treated with tofacitinib

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Abstract

We describe a case of refractory pouchitis successfully treated with tofacitinib. The patient was a 20-year-old woman diagnosed with ulcerative colitis at the age of 14 years. She underwent surgery at the age of 18 years for chronic active inflammation, despite an optimal medication regimen. Ten months after surgery, she was diagnosed with pouchitis. She did not respond to conventional conservative treatment; thus, the case was considered as that of refractory chronic pouchitis. Anti-tumor necrosis factor-α (TNF-α) therapy was administered, which led to some improvement; however, pouchitis recurred. Systemic steroid and vedolizumab were also administered, but the response was unsatisfactory. Therefore, surgery was considered; however, the patient refused to undergo surgery. As identical therapies are recommended for ulcerative colitis and pouchitis, they are considered to have a common etiology. Therefore, we considered tofacitinib therapy in this case. After obtaining the patient's informed consent, tofacitinib treatment was initiated. The therapy led to improvement in her symptoms as well as in the appearance of the pouch when observed on endoscopy, and surgery was avoided. Thus, tofacitinib may be considered a therapy option for refractory chronic pouchitis.

Keywords Pouchitis · Tofacitinib · Ulcerative colitis

Introduction

Pouchitis is a complication that develops following total proctocolectomy with the creation of a small bowel reservoir ileal pouch. The pathogenesis of pouchitis remains unknown. Approximately, 20–50% of patients who undergo proctocolectomy for ulcerative colitis develop pouchitis [1, 2] Further, more than 10% of patients with pouchitis develop chronic pouchitis, which is refractory to conventional treatment, including antibiotics and aminosalicylate [3].

Guidelines for the treatment of chronic refractory pouchitis differ in various countries. However, most therapies are common with those for ulcerative colitis [4, 5]. Anti-tumor necrosis factor-α (TNF-α) agents such as infliximab, apheresis, or calcineurin inhibitors are included in the guidelines. Recently, the effectiveness of vedolizumab for pouchitis has also been reported [6, 7].

Pouchitis that is non-responsive to any of the above therapies requires surgical excision and permanent diversion.

Tofacitinib is a Janus kinase (JAK) inhibitor that has been approved for the treatment of ulcerative colitis [8]. However, there are only one report described about its efficacy in pouchitis.

We describe a case of chronic pouchitis, which was refractory to other therapies but responded to tofacitinib. Surgical excision and permanent diversion of the pouch can adversely affect the quality of life of patients; therefore, more options for the conservative treatment of pouchitis are required.

Case report

A 20-year-old woman was diagnosed with left-sided ulcerative colitis at the age of 14 years. She had intolerance to aminosalicylate, and the condition was refractory to therapy with steroid, infliximab, adalimumab, and tacrolimus. Therefore, she underwent proctocolectomy with the creation of a small bowel reservoir-ileal pouch at the age of 18 years. Ten

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months after surgery, she complained of frequent diarrhea and abdominal pain.

Endoscopy revealed erosions and ulcers in the pouch, and she was diagnosed with pouchitis. Due to intolerance for aminosalicylate, she was administered metronidazole and ciprofloxacin; however, there was no improvement. Budesonide enema was added to the therapy; however, she did not respond to this regimen either. We diagnosed it as a refractory chronic pouchitis, and she was treated with infliximab, along with azathioprine. Infliximab reduced the frequency of bowel movements and abdominal pain. However, she developed a severe adverse reaction with dyspnea following the second infusion; therefore, infliximab was discontinued. Subsequently, golimumab therapy was administered, which proved effective. However, 6 months later, there was aggravation of hematochezia, abdominal pain, and frequency of bowel movements. Pouch endoscopy revealed deterioration of the ulcer and erosions in the pouch (Figs. 1a, b; 2). Tacrolimus therapy was considered; however, tacrolimus therapy administered before proctocolectomy had resulted in increased serum potassium. Therefore, systemic steroid therapy was considered for treating the pouchitis. Neither steroids nor vedolizumab proved effective; thus, surgery was considered. However, surgery would involve excision and permanent diversion of the pouch; thus, the patient refused to undergo surgery.

As the recommended therapies for pouchitis and ulcerative colitis are identical, it is probable that both have a common etiology. Therefore, we considered tofacitinib therapy in this case.

After obtaining informed consent from the patient and her family, we initiated tofacitinib therapy (Table 1). There was rapid improvement in the symptoms such as abdominal pain, frequency of bowel movements, and hematochezia, and her C-reactive protein reduced to normal levels and the modified pouchitis disease activity index (PDAI) [9] improved from 10 to 3 (Fig. 3). Six months after the initiation of tofacitinib therapy, an improvement in pouchitis was seen upon observation on endoscopy (Fig. 4 a, b).

The patient is currently under tofacitinib therapy for 7 months and is in a state of remission with no adverse events.

Discussion

Refractory chronic pouchitis is one of the most common causes of pouch failure. Common therapies for ulcerative colitis, including anti-TNF agents, are known to be effective for refractory chronic pouchitis. Though infliximab has been reported to be clinically effective in 80% of the cases over a short period and in approximately 50% of the cases over a long period [5], limited data are available about therapies including adalimumab or calcineurin inhibitors. Thus, it is very challenging to treat refractory chronic pouchitis cases

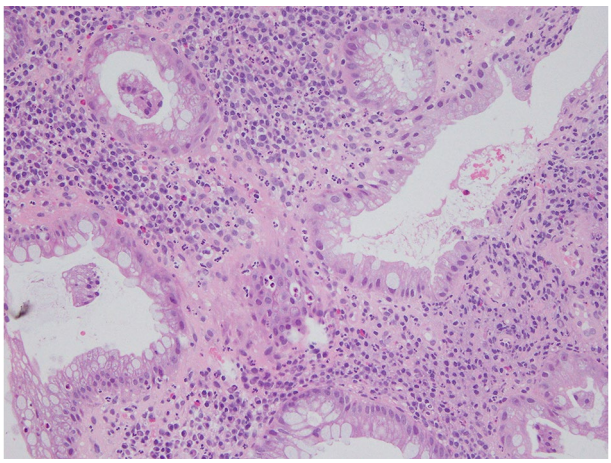

Fig. 2 Histopathology of biopsy from pouch. Diffuse infiltration of inflammatory cells is present in the lamina propria. There is no coincidence of cytomegalovirus infection

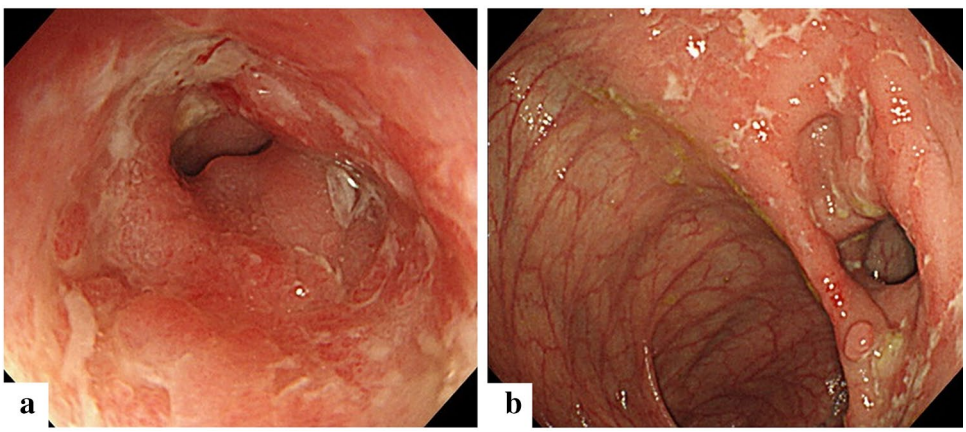

Fig. 1 Endoscopic appearance of pouchitis before treatment with tofacitinib. **a** Inflamed lesion of the pouch-pouchitis; **b** inflamed lesion of the anal canal-cuffitis

Table 1 Laboratory findings (just before initiating tofacitinib)

Hematology								
WBC	10.81	$\times 10^3/\mu L$	RBC	389	$\times 10^4/\mu L$	Plt	54.3	$\times 10^4/\mu L$
Neutrophils	67.0	%	Hb	9.2	g/dl			
Monocytes	5.5	%	Ht	29.7	%			
Eosinophils	4.0	%	MCV	76.3	fl			
Basophils	0.5	%	MCH	23.7	pg			
Lymphocytes	23.0	%	MCHC	31.0	%			
Biochemistry								
Total protein	6.9	g/dl	Total bilirubin	0.3	mg/dl	ESR(1 hr)	68	mm
Albumin	3.3	g/dl	Amylase	48	IU/l			
AST	10	IU/l	BUN	10	mg/dl			
ALT	4	IU/l	Cre	0.42	mg/dl			
LDH	150	IU/l	Na	136	mEq/l			
CK	13	IU/l	K	4.5	mEq/l			
ChE	204	IU/l	C	105	mEq/l			
ALP	170	IU/l	FBS	76	mg/dl			
γGTP	11	IU/l	CRP	2.3	mg/dl			

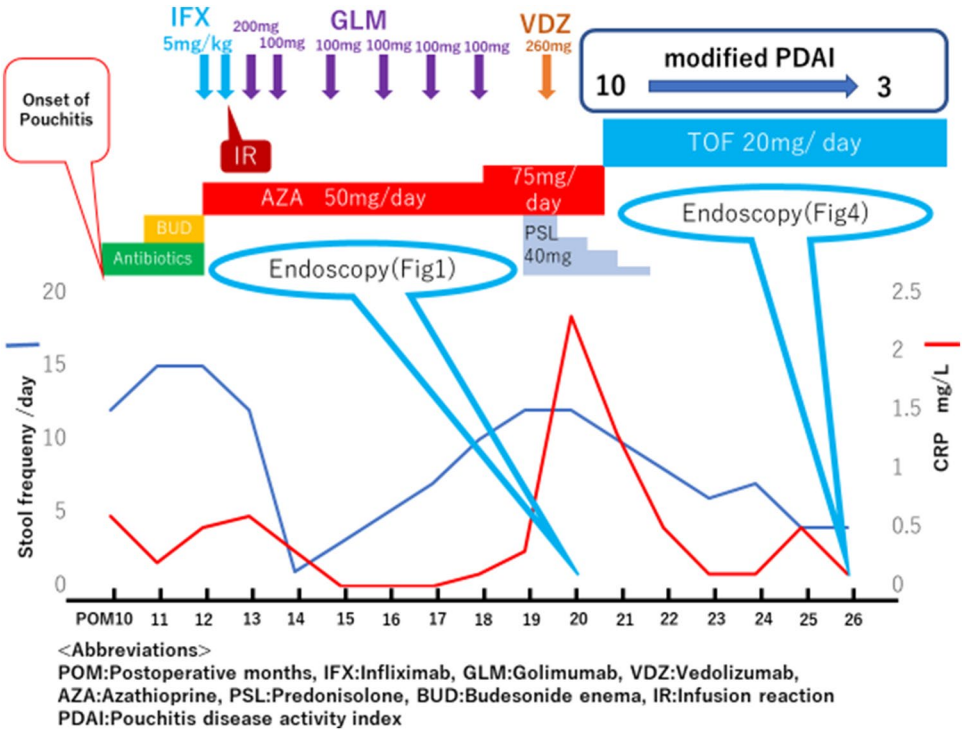

Fig. 3 Timeline of the clinical course and clinical findings during the treatment of pouchitis

that do not go into a state of remission following infliximab therapy.

Tofacitinib is a JAK inhibitor that inhibits the JAK pathway and reduces the production of inflammatory cytokines [10]. Its efficacy in the induction and maintenance of remission of ulcerative colitis was proven in the OCTAVE studies [8].

Malignancies and infections are the major risks of treatment with tofacitinib. However, treatment with tofacitinib for a few years revealed that the risks were similar to those associated with other biologic agents, except for the risk of herpes zoster infections [11]. Thus, treatment with tofacitinib can be considered relatively acceptable.

Recommended therapies for refractory chronic pouchitis and ulcerative colitis are identical, and a similar immune abnormality is considered to be associated with the etiologies of both the conditions. Therefore, tofacitinib might also be effective for refractory chronic pouchitis.

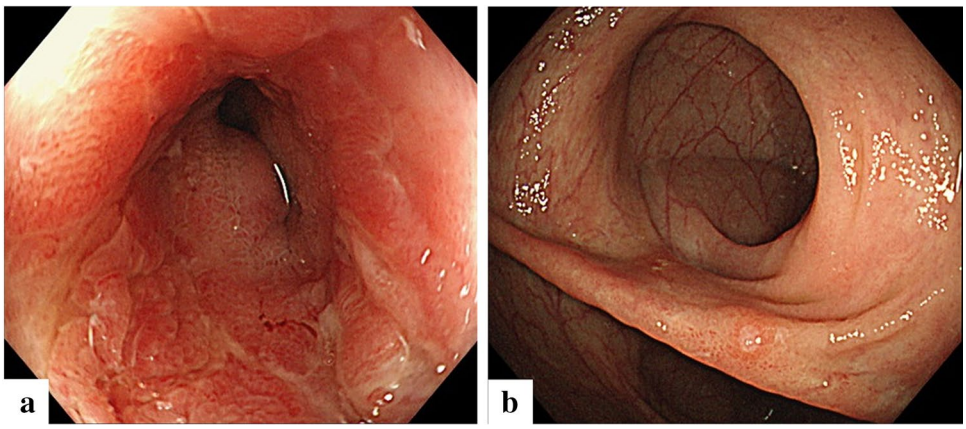

Fig. 4 Endoscopic appearance of pouchitis after treating with tofacitinib. **a** Inflamed lesion of the pouch-pouchitis; **b** inflamed lesion of the anal canal-cuffitis

There is only one case of refractory pouchitis treated with tofacitinib, which has been reported in an observational study [12]. However, its details are unknown.

In this case, Tofacitinib provided rapid improvement in the symptoms, and endoscopy of the pouch confirmed improvement in the disease condition. Currently, the patient continues to be in remission with tofacitinib treatment.

During surgery for refractory chronic pouchitis, surgical excision of the pouch and permanent diversion are usually performed, which can deteriorate the patient's quality of life. Therefore, it is necessary to uncover more options for conservative treatment in such patients.

In conclusion, this was a case in which tofacitinib was effective in the treatment of refractory chronic pouchitis, which did not respond to steroids and anti-TNF therapy. Tofacitinib can be considered as a new treatment option for patients with refractory chronic pouchitis.

Compliance with ethical standards

Conflict of interest Naoki Yoshimura received lecture fees from MOCHIDA PHAMACEUTIAL CO LTD. Mitsubishi Tanabe Pharma Corporation. AbbVieGK

Ethical approval All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from all patients for being included in the study.

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