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CASE REPORT

Successful Fistula Closure After Treatment with Colostomy and Infliximab in a Patient with Ulcerative Colitis Complicated by Rectovaginal Fistula

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Abstract: The patient was a 50-year-old Japanese woman who was diagnosed with total-colitis-type ulcerative colitis (UC) at the age of 26 years. She was treated with mesalazine and azathioprine, and her disease activity was well controlled. At the age of 50 years, the patient was experiencing fever, abdominal pain, diarrhea, bloody stool, and anal pain, which led to a diagnosis of a relapse of UC. Although steroid therapy was administered and tended to improve her symptoms, fecaloid vaginal discharge occurred, and rectovaginal fistula (RVF) was confirmed. Colostomy was performed, and infliximab was initiated as maintenance therapy for UC. All symptoms improved, and RVF closure was confirmed 6 months after the initiation of infliximab. To date, she has been free from relapse of UC. There have been only a few reports of UC complicated by RVF, and this condition is often difficult to treat. To the best of our knowledge, no other case of UC complicated by RVF in which the fistula was closed after treatment with colostomy and infliximab has been previously reported; thus, our report of the present case is valuable to the literature.

Keywords: ulcerative colitis, rectovaginal fistula, infliximab, colostomy

Introduction

Rectovaginal fistula (RVF) is defined as a tract covered with epithelium that communicates between the rectum and vagina.[1] The common symptoms include dyspareunia due to discharge of air and feces from the vagina, perianal pain, vaginal inflammation, and genitourinary system infections. These symptoms are recurrent and have a substantial impact on social and sexual life.[2,3]

The most common cause of RVF is obstetric trauma, and other frequently reported causes include pelvic surgery, malignant tumors, inflammatory bowel disease (IBD), and radiotherapy.[4] Regarding the association between IBD and RVF, the cumulative risk of developing RVF is 10% in women with Crohn's disease (CD), whereas the development of RVF is rare in women with ulcerative colitis (UC). There is no standard treatment protocol for RVF.[4]

Case Report

The patient was a 50-year-old Japanese woman who was diagnosed with total-colitis-type UC at the age of 26 years. She was treated with mesalazine and azathioprine, and her disease activity was well controlled. At the age of 50 years, the patient complained of bloody stools in addition to increased frequency of bowel movements (10 times/day). Pain occurred in the vaginal and anal areas. Abdominal computed tomography (CT) showed continuous edematous wall thickening from the sigmoid colon to the rectum (Figure 1). Abdominal magnetic resonance imaging (MRI) showed

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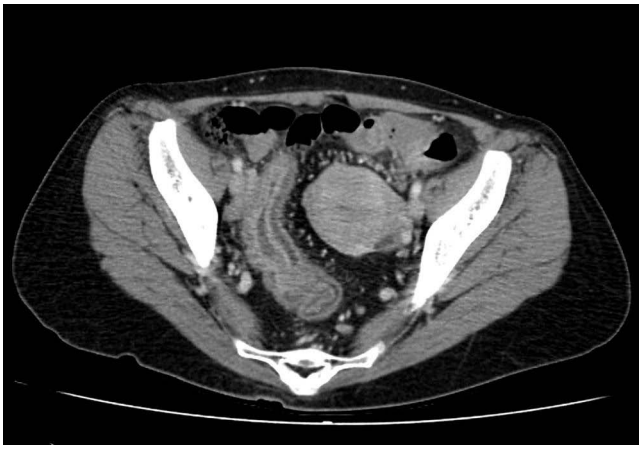

Figure 1 Abdominal CT showed continuous edematous wall thickening from the sigmoid colon to the rectum.

a continuous hyperintense area from the inside of the anal canal to the dorsal aspect of the vaginal wall on T2-weighted images (Figure 2). However, gynecological examination did not detect RVF. Although mesalazine suppository was added to her drug regimen, little improvement was achieved. Two months later, lower abdominal pain and fever developed in addition to anal pain. Hematologic tests showed a C-reactive protein (CRP) level of 70.5 mg/L, which was indicative of increased inflammation. Sigmoidoscopy revealed extensive mucosal sloughing and sporadic deep ulcers in the area from the sigmoid colon to the rectum (Mayo endoscopic subscore; MES[5] 3) but did not identify the opening of the fistula (Figure 3). The histopathological findings of biopsied colonic mucosa were consistent with relapse of UC. The results of fecal bacterial culture were negative for cytomegalovirus antigen and *Clostridium difficile* antigen/toxin. Because the Lichtiger colitis activity index[6] (CAI) score was 14 (diarrhea, 4; nocturnal diarrhea, 1; visible blood in stool, 2; fecal incontinence, 0; abdominal pain or cramping, 2; general well-being, 4; abdominal tenderness, 1; and need for antidiarrheal drugs, 0), the patient was diagnosed as having severe UC and hospitalized.

Intravenous infusion of prednisolone at a dose of 40 mg/day (1 mg/kg) was initiated. Although her CAI score and CRP level were markedly improved, fecaloid vaginal discharge was detected on day 8. Gynecological examination showed RVF on the dorsal aspect of the vagina at 1.0–1.5 cm from the vulva, with a size of 1.0 cm (Figure 4). Prednisolone was tapered down by 10 mg per week. On day 27, when the prednisolone dose reached 10 mg/day,

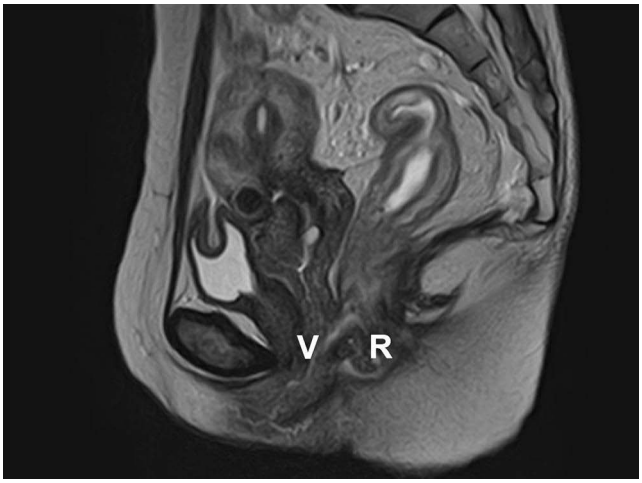

Figure 2 Abdominal MRI showed a continuous hyperintense area from the inside of the anal canal to the dorsal aspect of the vaginal wall on T2-weighted images.
Abbreviations: R, rectum; V, vagina.

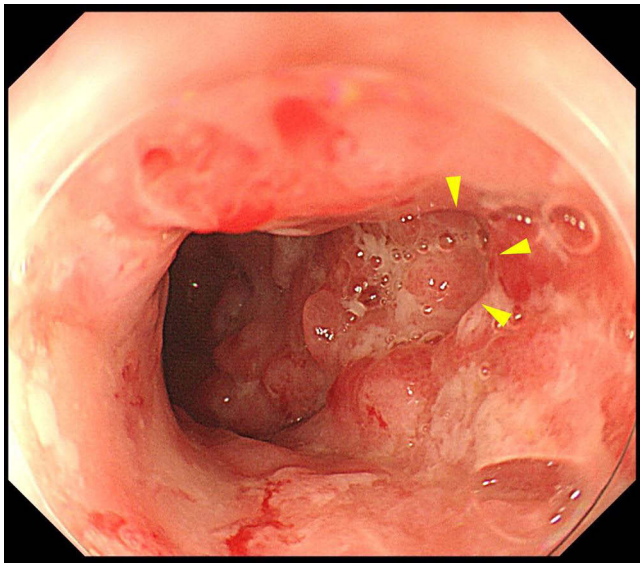

Figure 3 Sigmoidoscopy revealed deep ulceration (arrowheads) near the dentate line (Mayo endoscopic subscore 3) but did not identify the opening of the fistula.

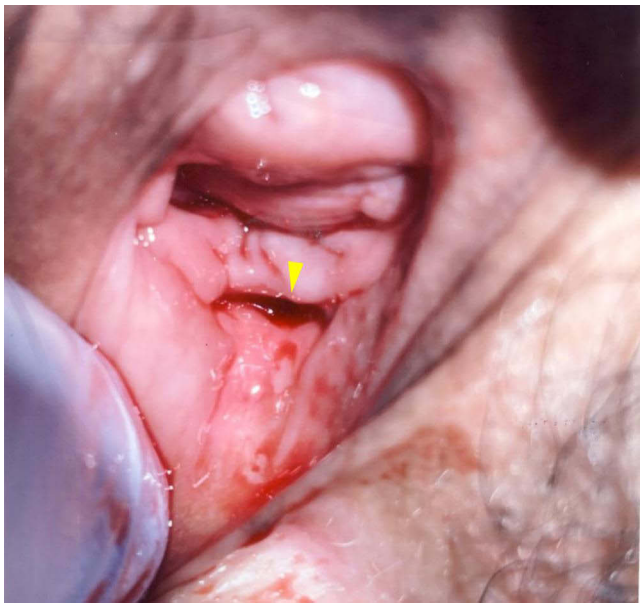

Figure 4 Gynecological examination showed rectovaginal fistula (arrowhead) on the dorsal aspect of the vagina at 1.0–1.5 cm from the vulva, with a size of 1.0 cm.

laparoscopic transverse colostomy was performed. Her postoperative course was favorable, and the patient was discharged on day 36.

Infliximab was initiated as maintenance therapy for UC at the outpatient clinic, and prednisolone was discontinued approximately 2 months later. Six months after the initiation of infliximab, gynecological examination confirmed RVF closure (Figure 5). Colonoscopy showed improvement of colonic mucosal inflammation (MES 1, Figure 6), and her CAI score also improved to 2 (diarrhea, 1; nocturnal diarrhea, 0; visible blood in stool, 0; fecal incontinence, 0; abdominal pain or cramping, 0; general well-being, 1; abdominal tenderness, 0; and need for antidiarrheal drugs, 0). Infliximab is still administered every 8 weeks to date, and no relapse of UC has been observed. Future closure of the stoma is being considered.

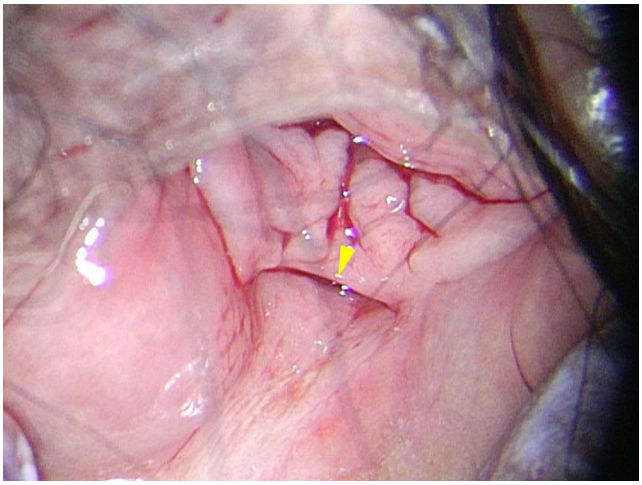

Figure 5 Gynecological examination confirmed the closure of rectovaginal fistula (arrowhead).

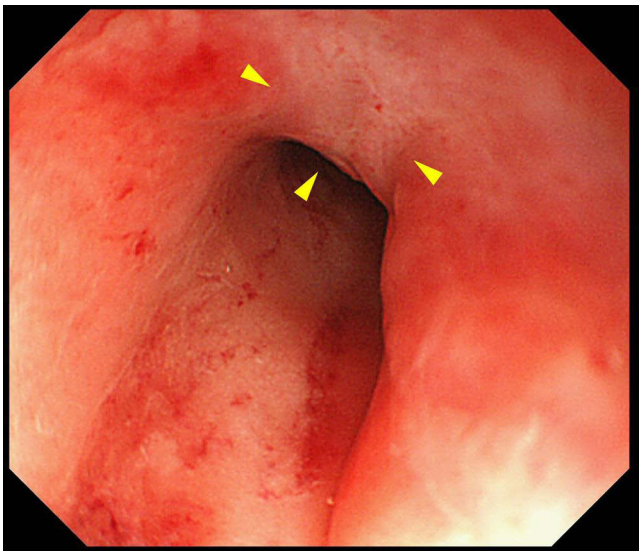

Figure 6 Colonoscopy showed improvement of colonic mucosal inflammation (Mayo endoscopic subscore 1). An ulcer near the dentate line was scarred (arrowheads).

Discussion

Rectovaginal fistula is treated with various procedures in consideration of the etiology, as well as the size and location of the fistula, conditions of the anal sphincter complex and surrounding tissues, presence or absence of inflammation, and patient conditions. The treatment procedures that are attempted include drainage seton, fibrin glue application, endorectal or vaginal advancement flap, episioproctotomy, transverse transperineal repair, fistulectomy and closure, Martius (bulbocavernosus) flap, gracilis muscle flap, interposition of levator ani muscles, and abdominal procedures with colorectal or coloanal anastomosis.[7,8] Regarding treatment outcomes for primary diseases causing RVF, the closure rate after treatment of IBD is as low as 46.1%–60.0%.[9,10] Thus, RVF in patients with IBD often requires repeated surgery to achieve complete cure, and most patients ultimately undergo ileostomy or proctocolectomy.[11]

To improve the low closure rate of RVF, pharmacotherapy has been a standard treatment approach, particularly for RVF complicating CD. The principle of pharmacotherapy is to suppress the activity of underlying diseases. Current medications used to treat CD with anal lesions include antibiotics, corticosteroids, immunomodulators, and biopharmaceuticals.[12] However, there have not been randomized controlled trials that support the use of antibiotics, and most evidence has been derived from small-scale studies. Metronidazole is used primarily, and often in combination

with immunomodulators.[13] Metronidazole acts on intestinal flora to exert its inhibitory effect on toxic bacteria while increasing beneficial bacteria. This effect has been shown to lead to closure of some perianal fistulas.[14] However, neurologic adverse drug reactions to metronidazole limit its long-term use.[15,16]

Immunomodulatory therapies for fistula complicating CD include cyclosporine,[17,18] 6-mercaptopurine,[19] and azathioprine.[20,21] In the studies using these drugs, continuous treatment was difficult because fistula often recurred and various adverse events were observed over time. Thus, before 2000, the existing therapies for RVF complicating IBD had been poorly effective, necessitating newer strategies with greater efficacy.

In 2004, Sands et al conducted the first and only randomized controlled trial (A Crohn's Disease Clinical Trial Evaluating Infliximab in a New Long-Term Treatment Regimen in Patients with Fistulizing Crohn's Disease [ACCENT II trial]) that evaluated the efficacy of infliximab therapy for fistulizing CD. The fistula closure rate was 36% in the infliximab group, which was higher than 19% in the placebo group.[22] In the post-hoc analysis of the ACCENT II trial, which evaluated the effect of infliximab therapy for closure of external fistulas, 44.8% of patients with RVF achieved fistula closure 14 weeks after the initiation of infliximab therapy. Furthermore, when patients who responded to induction therapy with infliximab were randomly assigned to maintenance therapy with infliximab or placebo, the median duration of RVF closure was longer in the treatment (46 weeks) than in the placebo (33 weeks) group.[23]

In a systematic review of 137 patients from 23 studies on CD-associated RVF, the overall cure rate for pharmacotherapy was 38.3%, whereas the cure rates were 41.0% for anti-tumor necrosis factor-alpha (TNF-α) antibody therapy and 44.2% for a combination of medical and surgical treatments.[24] Based on the studies described above, the European Crohn's and Colitis Organization guidelines state that the repair of CD-associated RVF is difficult and that the selection between medical treatment in combination with surgical treatment and surgical treatment alone should be considered on a case-by-case basis by a multidisciplinary team of experts.[25]

In both UC and CD, TNF-α has been shown to increase during the active phase of inflammation,[26] which suggests the efficacy of anti-TNF-α antibody formulations. Previous reports have presented cases of successful fistula closure with adalimumab for UC-associated RVF in patients without any history of surgery[27] and cases of successful fistula closure with infliximab for RVF after ileoanal canal anastomosis in patients with UC.[28] Regarding the effectiveness of colostomy, it has been reported that colostomy accelerates RVF closure.[10] The reason is that fecal diversion is thought to reduce the bacterial load around the anus and help improve healing conditions.[29] On the other hand, the presence of a large fistula and pelvic sepsis are two important predictors of failure of fecal diversion alone.[30] Therefore, after colostomy, concomitant or subsequent repair of the RVF is recommended for patients with these two risk factors.

In this case, we believe that her RVF was caused by a deep ulcer in the rectum. The size of RVF is an important factor in the choice of treatment, as the diameter of the fistula is classified as small (<0.5 cm), medium (0.5–2.5 cm), and large (>2.5 cm).[8] The size of her RVF confirmed from the vaginal side is 1.0 cm, indicating that her RVF as medium size and we expected it was difficult to repair with single treatment. Because of that, we chose colostomy and infliximab treatment.

Conclusion

Ulcerative colitis complicated by RVF is extremely rare. However, when RVF occurs, it is difficult to treat. At present, no optimal therapeutic strategies have been established, but we believe that it is important to select the treatment method according to the size of RVF. A combination of colostomy and infliximab contributed to fistula closure and long-term maintenance of closure for RVF and was suggested to be one of the potentially useful therapeutic options for medium size RVF.

Abbreviations

UC, ulcerative colitis; RVF, rectovaginal fistula; IBD, inflammatory bowel disease; CD, Crohn's disease; CT, computed tomography; MRI, magnetic resonance imaging; CRP, C-reactive protein; MES, Mayo endoscopic subscore; TNF, tumor necrosis factor.

Institutional Approval

No institutional approval was required for the publication of this manuscript.

Ethical Considerations

Written informed consent was obtained from the patient for publication of this Case Report and the accompanying images.

Disclosure

The authors report no conflicts of interest in this work.

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