Treatment of a Case of Ulcerative Colitis with Sacroiliitis Using Granulocyte and Monocyte Adsorption Apheresis

Hitoshi ICHIKAWA[*1], Jin IMAI[*1], Hajime MIZUKAMI[*2], Takayuki SHIRAI[*1] and Norihito WATANABE[*1]

[*1]*Division of Gastroenterology and Hepatology, Department of Internal Medicine, Tokai University Hachioji Hospital*
[*2]*Division of Gastroenterology and Hepatology, Department of Internal Medicine, Tokai University School of Medicine*

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In Japan, sacroiliitis is a very rare extraintestinal manifestation in patients with ulcerative colitis (UC), and it typically presents with intestinal symptoms. Radiography is used for diagnosis, and reveals erosions, sclerosis, and ankylosis, but magnetic resonance imaging is more useful for early detection.
The treatment of spondyloarthropathy such as sacroiliitis and spondylitis includes physiotherapy, nonsteroidal anti-inflammatory drugs, sulfasalazine, and immunomodulators. In patients intolerant or cases refractory to these treatments, anti-tumor necrosis factor agents are recommended. Granulocyte and monocyte adsorption (GMA) apheresis was developed in Japan in the 1980s, and is currently used widely in clinical practice for UC patients. Unlike conventional medication, GMA apheresis has no serious adverse effects. We present the first report of a UC patient with sacroiliitis, who responded well to GMA therapy. GMA apheresis may be considered a new treatment option for UC-associated spondyloarthropathy that is refractory or tolerant to conventional treatment.

Key words: sacroiliitis, spondyloarthropathy, ulcerative colitis, granulocyte and monocyte adsorption apheresis

INTRODUCTION

Sacroiliitis is a rare extraintestinal manifestation of ulcerative colitis (UC), which occurs with a prevalence of 0.03−0.07% in Japan [1, 2]. The treatment of spondyloarthropathy (SpA) such as sacroiliitis and spondylitis includes physiotherapy, nonsteroidal anti-inflammatory drugs (NSAIDs), sulfasalazine, and immunomodulators. In patients intolerant or cases refractory to these treatments, anti-tumor necrosis factor (TNF) agents are recommended. These treatments have some disadvantages. For example, NSAIDs can precipitate flares of UC, sulfasalazine does not have an immediate therapeutic effect, and immunomodulatory or anti-TNF agents are associated with an increased risk of opportunistic infection.

Granulocyte and monocyte adsorption (GMA) apheresis was developed in Japan in the 1980s, and is currently used widely in clinical practice for UC patients. There have been no reports of serious adverse effects of GMA apheresis, including opportunistic infections. Several prior studies have identified the clinical benefit of GMA apheresis for pyoderma gangrenosum, which is one of the extraintestinal manifestations of UC [3−5]. We hypothesized that articular manifestations of UC could be controlled when intestinal inflammation was controlled. We report a patient with UC and sacroiliitis, who responded well to GMA apheresis therapy.

CASE REPORT

A 20-year-old man with UC who had taken sulfasalazine for the prior year was referred to our hospital with one week of bilateral hip joint pain. He reported passing slightly bloody stools twice a day. He had a prior history of sacroiliitis associated with UC. He was diagnosed with sacroiliitis and a mild flare of UC, and was started on a cyclooxygenase-2 (COX-2) inhibitor. However, he did not respond well, and was hospitalized 11 days later. On admission, he complained of claudication and restriction of movement of the hip joints, and reported 6 bloody stools a day, with intermittent lower abdominal cramping. Laboratory examination showed an hemoglobin level of 15.0 g/dl, white blood cell count of 10,900/μl, albumin level of 3.4 g/dl, and C-reactive protein level of 2.5 mg/dl. Results of tests for HLA-B27 and antinuclear antibody were negative. Short tau inversion recovery (STIR) axial pelvic magnetic resonance imaging (MRI) showed some high intensity areas in the bilateral sacroiliac joints, indicating bone marrow edema, and he was diagnosed with sacroiliitis (Figure A). The European Crohn's and Colitis Organisation guidelines reported the safety of COX-2 inhibitors, with a lower risk of UC flares [6]. Therefore, administration of the COX-2 inhibitor was continued, and GMA apheresis therapy was administered twice a week, for a total of 5 sessions. Bilateral hip joint pain rapidly disappeared, with improvement of abdominal symptoms following the 2nd session of GMA apheresis. STIR axial pelvic MRI revealed a

Hitoshi ICHIKAWA, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Tokai University Hachioji Hospital, 1838 Ishikawa-machi Hachioji, Tokyo 192-0032, Japan Tel: +81-42-639-1111 Fax: +81-42-639-1144 E-mail: ih0319@tokai.ac.jp

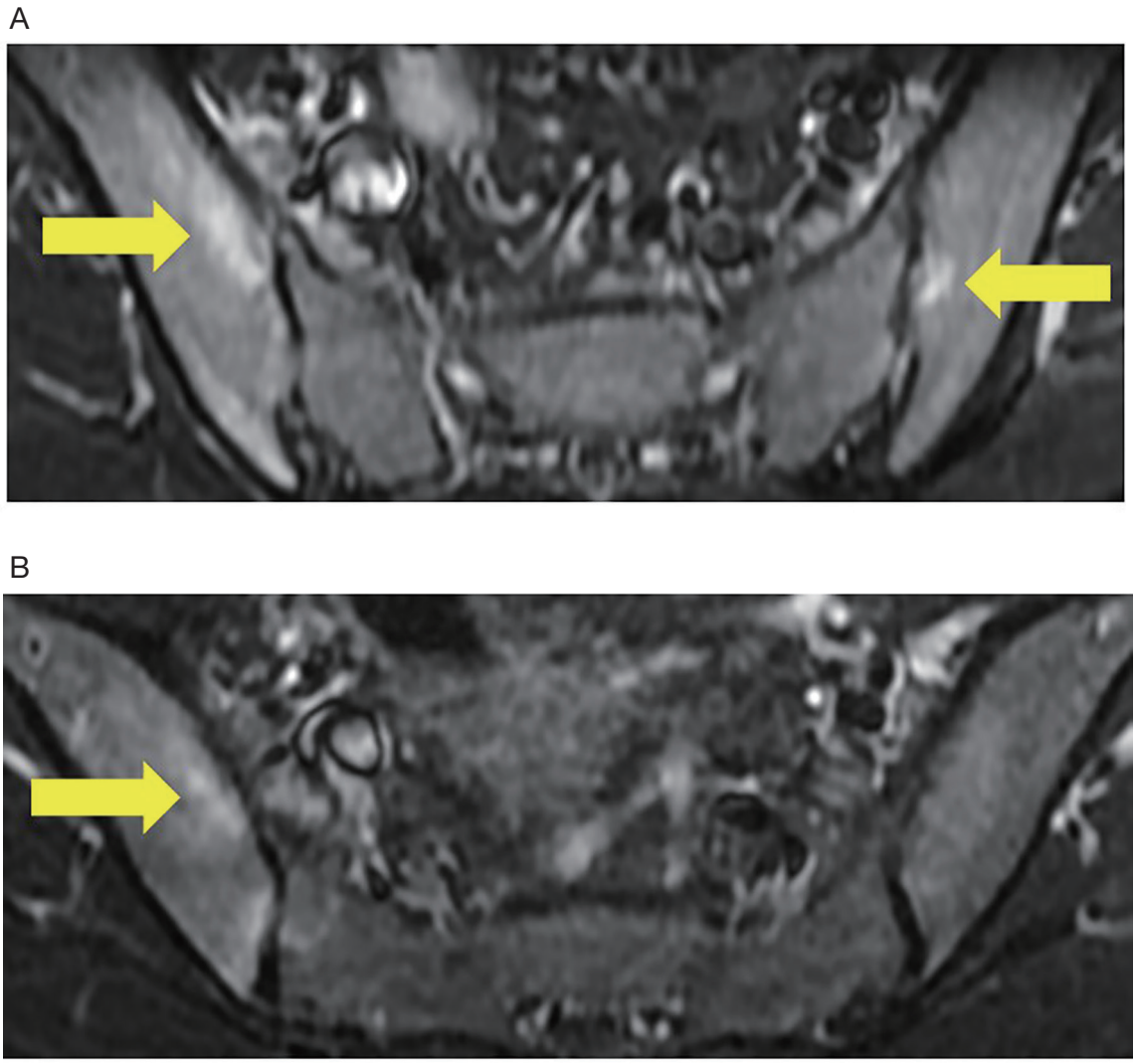

Figure Axial STIR pelvic magnetic resonance imaging demonstrating high intensity signal (arrow) in the sacroiliac joint. (A) Before GMA apheresis. (B) After GMA apheresis
STIR, short tau inversion recovery; GMA, granulocyte and monocyte adsorption.

decrease in high-intensity lesions by the 5th session of GMA apheresis (Figure B). The patient was discharged without claudication on day 16. With GMA apheresis, he recovered from UC associated sacroiliitis three times in the past two years, including this second episode.

DISCUSSION

To the best of our knowledge, this is the first report of the efficacy of GMA apheresis in a UC patient with sacroiliitis. GMA apheresis has both an immediate therapeutic effect and an excellent safety profile for articular and intestinal symptoms of UC. The main adverse effects of GMA apheresis are headache, dizziness, nausea, and mild fever. These adverse effects were noted in 36 of 670 UC patients (5.5%), and were all mild and transient [7]. Although the precise mechanism of GMA apheresis is not yet understood [8–10], it is known to affect both the quantity and quality of granulocytes and monocytes. GMA apheresis selectively removes neutrophils from the peripheral blood, and their concentration in inflamed areas decreases. In addition to reducing their number, the contact of peripheral blood mononuclear cells with cellulose acetate beads results in the reduction of proinflammatory TNF-α, interleukin (IL)-1β, IL-6, and IL-8 production [11]. Intestinal inflammation, which is mainly subclinical, is present in about 60-70% of SpA patients without intestinal symptoms, and some of these subsequently develop inflammatory bowel disease [12, 13]. The activity of SpA is correlated with that of intestinal inflammation [12, 14]. GMA apheresis may have a beneficial effect on articular activity by controlling intestinal inflammation.

We should note that we did not administer systemic glucocorticoids in our patient. In adult patients with active sacroiliitis refractory to NSAIDs, treatment with parenteral glucocorticoids is recommended in Western countries [15]. In Japan, only a few reports have indicated the efficacy of systemic glucocorticoids in UC patients with sacroiliitis [16, 17]. The common clinical finding in patients with active sacroiliitis who respond well to systemic glucocorticoids is a positive antinuclear antibody test, which was absent in this case.

In conclusion, GMA apheresis may be considered a new treatment option for UC-associated SpA that is refractory or tolerant to conventional treatment.

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