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□ Case Report □

Localized Gastrocnemius Myositis in Crohn's Disease

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We describe a case of localized gastrocnemius myositis which developed with flare-up of Crohn's disease. A 21-year old male patient with an 8-year history of Crohn's disease presented with pain and tenderness in both calves without recent abdominal symptoms. Electromyography and gastrocnemius muscle biopsy revealed evidence of inflammatory myositis. Magnetic resonance imaging (MRI) showed bilateral symmetrical diffuse increased signal intensity in T2 weighted images in both gastrocnemius muscles and patchy contrast enhancement. Subsequent gastrointestinal investigation revealed active inflammation of colon with multiple pseudopolyps and enteroenteric fistula on which we commenced oral prednisolone of 30 mg daily. His pain on both calves was improved and muscle enzymes became normal. Following dose reduction of prednisolone, azathioprine 50 mg daily was started considering the patient's active Crohn's disease on endoscopic findings prior to the development of overt abdominal symptoms. This is the first case report of localized gastrocnemius myositis associated with Crohn's disease described in Korea. Calf myositis responded to corticosteroid well and did not recur with maintenance therapy using azathioprine and mesalazine.

Key Words. **Localized gastrocnemius myositis, Crohn's disease, Inflammatory bowel disease, Magnetic resonance**

Introduction

Musculoskeletal involvement is a common extraintestinal manifestation of inflammatory bowel disease (IBD) (6～64%) which includes pauci-, poly-arthritis, myalgia, diffuse inflammatory myositis such as polymyositis, dermatomyositis enthesitis, localized joint pain, axial spondyloarthropathies and fibromyalgia-like symptoms (1).

Localized gastrocnemius myositis was is rare, but also described as one of typical extraintestinal manifestation of IBD. To date, nine cases of IBD related gastrocnemius myositis have been reported presenting calf-confined myalgia, which were preceding or following the diagnosis of IBD (2). Herein we report a patient with localized gastrocnemius myositis followed by a flare of Crohn's disease.

Case Report

A 21-year-old man presented with acute onset of pain and tenderness in both calves causing difficulty in ambulation for 1 month. He was referred to division of rheumatology. The patient denied any trauma nor any systemic symptom. He had a history of Crohn's disease for 8 years. He had experienced a flare related to Crohn's disease 7 years earlier with anal fistula, anorexia, diarrhea and weight loss of 12 kg, and endoscopic investigation had found typical lesions of Crohn's disease. After treatment with 40 mg of daily of oral prednisolone, mesalazine 500 mg three times daily, azathioprine 50 mg daily, metronidazole 250 mg three times daily since then, he was currently on remission status and the only medication he was taking were mesalazine three times daily without specific bowel symptoms. Colonoscopic findings of 1 year earlier to this event was normal.

On physical examination, significant tenderness in both calves without erythema or edema was noticed. He had no evidence of skin rashes, arthralgia, muscle weakness or sen-

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sory changes. Physical examination was otherwise unremarkable, with normal vital signs.

Laboratory values revealed a white blood cell count of 7,920/mm^3, a hemoglobin level of 10.2 g/dL, a platelet level of 316,000/mm^3 with a mildly elevated erythrocyte sedimentation rate of 41 mm/hr, and C-reactive protein of 1.51 mg/dL. Serum aldolase level was slightly elevated (13.9 U/L (< 7.5 U/L)), while serum creatinine kinase, myoglobin, lactate dehydrogenase levels were within normal range (30 U/L (20～270 U/L), 12.0 ng/ml (17.4～105.7 ng/ml), 160 IU/L (100～225 IU/L), respectively). Anti-neutrophil cytoplasmic antibody (ANCA) was negative, as were his proteinase 3-ANCA, myeloperoxidase-ANCA and anti Jo-1 antibody were negative.

Needle electromyography showed small amplitude and short duration of polyphasic motor unit potential and early recruitment with reduced interference in left gastrocnemius, which were consistent with acute myositis. Nerve conduction studies showed normal responses.

MRI of bilateral symmetrical diffuse increased signal intensity in T2 weighted images in both gastrocnemius muscles and patchy contrast enhancement that were consistent with an inflammatory myositis (Figure 1).

With these findings, muscle biopsy of the left gastrocnemius muscle was performed. Paraffin-embedded, hematoxylin-eosin-stained sections showed variation in size of the muscle fibers and degenerating or regenerating muscle fibers. Some inflammatory cell infiltrations were observed. There was no evidence of vasculitis. Immunohistochemistry revealed moderate CD56+ macrophage infiltrates distributed in regenerating fibers and CD4+ and CD8+ T cells infiltrates were found in perivascular and endomysial locations. Electromicroscopic ultrathin sections exhibited variable sizes of myofibers with degenerating and regenerating myofibers, which are mostly round in shape. Mild fibrosis with mild proliferation of fat layer in perimysium were observed. Mild infiltration of inflammatory cells in endomysium and perivascular are also present. Conclusively, biopsy results were consistent with polymyositis (Figure 2).

During a series of examination, colonoscopic investigation revealed multiple inflammatory polyp in transverse colon, as well as narrowing of the descending colon (Figure 3A). Small bowel barium enema showed cobble stone appearance over cecum, IC valve, terminal ileum and longitudinal ulcer along the mesenteric border of terminal ileum were observed (Figure 3B). Multifocal pseudosacculation in antimesenteric border with interpositioning of normal ileum were found. Irregular contrast leakage in right lower quadrant area was visible appa-

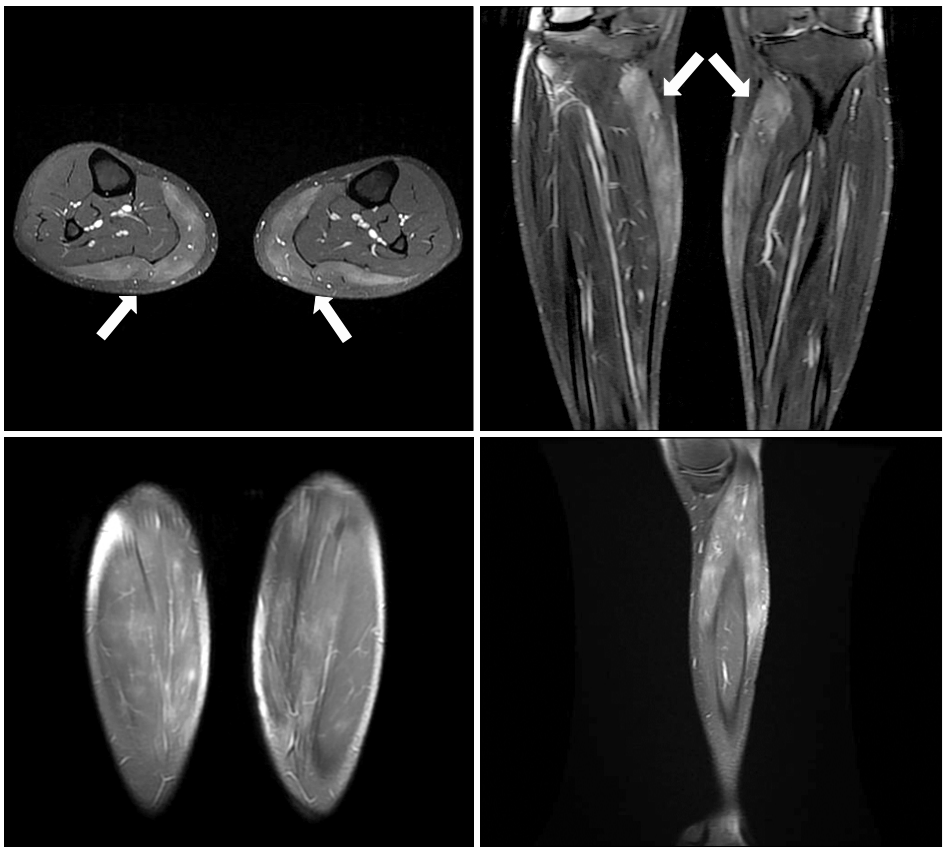

Figure 1. Both lower leg MRI showed bilateral symmetrical diffuse signal alteration of gastrocnemius muscles and patchy contrast enhancement (arrow) consistent with inflammatory myositis.

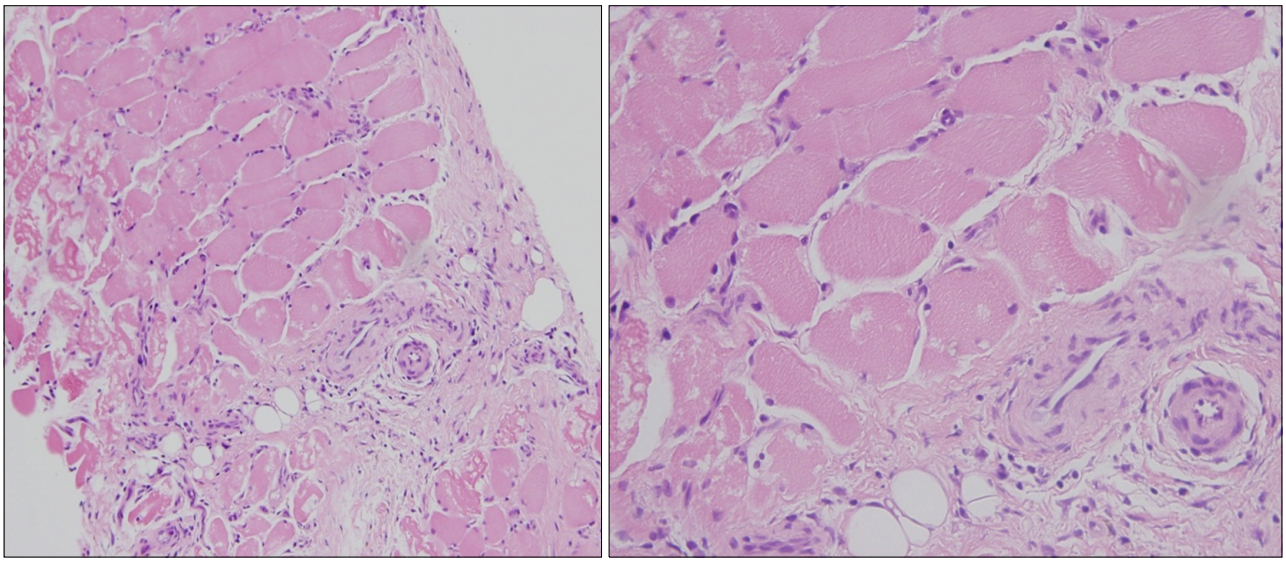

Figure 2. Biopsy of the left lateral gastrocnemius muscle revealed that there is a mild size variation of myofibers and inflammatory cell infiltration in the endomysium and perivsacular area. Some degenerating and regenerating myofibers are shown. Internal nuclei are not prominent. There is mild fibrosis and fat ingrowth in the endomysium but no evidence of vasculitis.

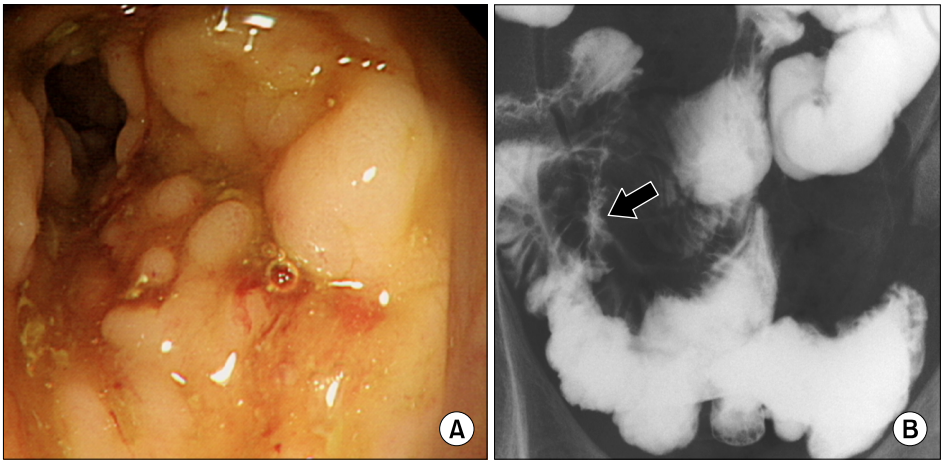

Figure 3. (A) Colonoscopy showing cobble stone appearance over cecum, IC valve, terminal ileum and longitudinal ulcer along the mesenteric border of terminal ileum were observed. (B) Small bowel barium enema showing multifocal pseudosacculation in the antimesenteric border with interpositioning of the normal ileum was found. Irregular contrast leakage in the right lower quadrant area were visible, apparently suggesting enteroenteric fistula confined to mesentery (arrow).

rently suggesting enteroenteric fistula confined to mesentery. These findings were also noticed on abdominal computed tomography with thickened wall with contrast enhanced of ascending colon, cecum and terminal ileum and enteroenteric fistula. With these results of gastrointestinal investigation, active stages of Crohn's disease were diagnosed.

The patient was started on oral prednisolone 30 mg daily (0.5 mg/kg/day). This decreased his pain on both calves along with improving laboratory findings of C-reactive protein, erythrocyte sedimentation rate and aldolase (Figure 4). Following stepwise reduction of the dose of prednisolone to 5 mg daily 2 months later, azathioprine 50 mg daily was started considering active stage of previous endoscopic finding of Crohn's disease.

One year later, the patient did not report recurrence of calf myalgia and did not show elevation of C-reactive protein, er-

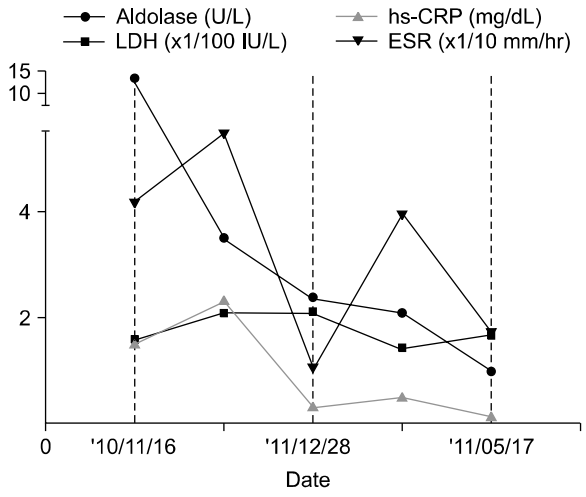

Figure 4. Serial changes in laboratory data.

ythrocyte sedimentation rate and aldolase. Though, the patient developed hematochezia one year later with uncontrolled active stage of Crohn's disease in repeated colonoscopic investigation including ulceration and narrowing of multiple lesions of colon. The patient continued to take prednisolone 5 mg daily, azathioprine 50 mg daily, mesalazine 500 mg three times daily.

Discussion

Gastrocnemius myalgia syndrome is rare extraintestinal manifestations, Up to date, 9 cases have been reported (2). To our knowledge this is the first case reported in Korea.

Musculoskeletal symptom preceded gastrointestinal symptom in most reported cases (2-4). Regardless of history of previous IBD, presence of any myopathy may herald a development or a flare of IBD such as Crohn's disease. Some had history of Crohn's disease before diagnosis of myositis as in our patient, while majority of cases did not (3). A case of polymyositis followed by Crohn's disease were reported in Hungary as well (4). Our patient with 6-year history of Crohn's disease had been stable for several years without gastrointestinal symptom taking only 5 mg daily of prednisolone. Endoscopic examination which was done in 1 year before the admission showed a remission status. Endoscopic examination, small bowel series and computed tomography after diagnosis of localized gastrocnemius myositis revealed an active stage of Crohn's disease and additive immunosuppressant were commenced consequently. In the literature, myopathy improved as ileocolonic inflammation reached remission with or without mesalazine or 5-ASA agents, and recurred during acute flare of IBD in most cases, suggesting that muscle symptom reflect clinical activity of IBD (5).

The only manifestation in our patient was myositis without any abdominal symptoms while endoscopic disease was active. It might suggest that extraintestinal manifestations, such as myositis like in this case, mirror disease activity of Cronh's disease which present only endoscopic disease without abdominal symptoms yet. We suggest that thorough gastrointestinal investigation should be done to seek any related condition. It may lead to diagnose the first presentation of Crohn's disease or notice the impending flare or active status prior to or regardless of overt symptoms. Most IBD patients in remission have low grade of inflammation and relapse could occurs when gut inflammation reaches upto high intensity. In asymptomatic stage, flare could be only predicted by direct assessment of the grade of inflammatory activity by endoscopic examination or documentation of inflammatory cell infiltrates in mucosal biopsy. Asymptomatic endoscopic disease without abdominal symptoms might be diagnosed in presymptomatic stage before clinical relapse. The role of fecal calprotectin or gut ultrasound in predicting endoscopic recurrence have been reported in asymptomatic Crohn's disease (6). In our case, it could be possible that endoscopic inflammation had recurred before overt abdominal pain or hematochezia in patient and so, myositis in both calves might be the first sign of flare in Crohn's disease.

Muscle symptoms associated Crohn's disease have been reported to respond well to glucocorticosteroid monotherapy, while reports of recurred or refractory diseases which exhibited recurrence following cessation of steroids described the use of combination of immunosuppressants (2). Mogul et al reported a case which responded to steroid initially but recurred subsequently to require methotrexate for complete resolution of myositis (2). Szabo et al. (4) reported a case which were refractory to steroid monotherapy and improved with a combination therapy of azathioprine and 5-ASA. In the present case, although myositis responded to the moderate dose of prednisolone, endoscopic disease persisted over duration of follow up. It seems that higher dose of steroids are required for controlling IBD. Azathioprine and mesalazine were added for purpose of controlling of colonic inflammation 2 months later. Maintenance therapy with immunosuppressant such as azathioprine or methotrexate to prevent recurrent myositis would be reasonable.

MRI demonstrated definite lesion confined to bilateral gastrocnemii with an increased signal on T2 weighted images in our patient. Although the gold standard for diagnosis is muscle biopsy of affected site, histopathologic results from localized gastrocnemius myositis cases have been reported to be heterogeneous including nonspecific myositis, granulomatous myositis or vasculitis and not to be related to treatment responses (2). Considering its typical presentation of calf-localised myalgia in IBD setting, noninvasive approach with MRI might substitute invasive biopsies.

It is not known why myositis associated with IBD is confined to gastrocnemii, possible explanation may be shared T-cell mediated inflammatory immune mechanism for both the bowel and muscle inflammation (2). Infectious agents such as *Campylobacter, Borrelia burgdorferi* or BCG vaccination have been suggested for triggering gastrocnemius myositis and it may be another start of explanations (7). There was no other muscle involvement in our patient except both calves.

Summary

In this case of localized gastrocnemius myositis, muscle symptom called on attending physician to embark gastrointestinal investigation prior to development of overt symp-

toms to find out active Crohn's disease. Localized myalgia on calf readily improved with initial steroid and did not recur with azathioprine maintenance therapy. Combined with a high index of suspicion, noninvasive MRI may alert the physician to the diagnosis of local myositis in the setting of IBD. Collaboration between gastroenterologists and rheumatologists for appropriate approach to musculoskeletal manifestations in IBD is demanded.

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