

**Familial Mediterranean Fever with Colonic Involvement Mimicking Inflammatory**

**Bowel Disease**

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A 42-year-old woman experienced recurrent febrile attacks (over 38°C) and diffuse abdominal pain that spontaneously subsided within two to three days, beginning in April 2009.

Laboratory data showed leukocytosis and elevated serum C-reactive protein. Colonoscopy revealed discontinuous loss of fine vascular markings, erythema, and friable mucosa in the right hemicolon. Biopsy specimens revealed no characteristic features related to Crohn's disease (CD) or ulcerative colitis (UC). CT scan showed wall thickness of colon. Capsule endoscopy revealed no abnormality in small intestine. ASCA and ANCA were negative.

Therefore, she was diagnosed with indeterminate colitis. 4g of mesalazine was firstly administered, and 1.5g was kept for maintenance. But her symptoms continued.

In July 2009, 40mg of prednisolone was orally administered to control her repeated episodes.

Her symptoms subsided, and the prednisolone dosage was tapered in August 2009. Her symptoms recurred, however, when the prednisolone dosage reached the 6-mg level.

Mercaptopurine could not be used because of her intolerance.

In April 2010, colonoscopy revealed circumferentially erythematous mucosa with erosions in the cecum, longitudinal erosions with pseudopolyposis-like lesions in the right hemicolon, and no involvement of the rectum. These endoscopic features resemble CD (Figure 1-A and

1-C), but biopsy specimens revealed no granuloma. Intestinal tuberculosis and other infectious diseases were ruled out.

She continued to have febrile attacks every week in May 2010. Moreover, her attacks were accompanied by severe abdominal pain as well as bilateral arthralgia in the wrists, elbows, and shoulders.

Because her symptoms met the Tel Hashomer criteria, we suspected familial Mediterranean fever (FMF). After obtaining written informed consent, we performed a genome sequencing examination for the Mediterranean fever gene (*MEFV*) mutation, which revealed a heterozygous *MEFV* mutation, a 910G>A point mutation. This mutation causes a Gly304Arg missense mutation on pyrin (Figure 2).

After diagnosing her with FMF in late May 2010, 1mg of colchicine was administered. Her symptoms promptly subsided, and we could stop prednisolone and mesalazine. In February 2011, colonoscopy revealed remarkable improvement of the mucosal inflammation in the colon (Figure 1-B and 1-D). In the two years since starting colchicine treatment, she has had no febrile attacks or serositic symptoms.

FMF is a periodic inflammatory disease characterized by episodic febrile attacks and serositis.

It is a monogenic Mendelian disease caused by *MEFV* on chromosome 16p13.3, which encodes pyrin.<sup>1</sup> Pyrin is a 781-amino-acid protein mainly expressed in granulocytes and monocytes,<sup>2</sup> and regulates the inflammatory response by blocking intracellular signal pathways via NF- $\kappa$ B or caspase 1. The absence of pyrin function due to mutated *MEFV* leads to the oversecretion of inflammatory cytokines, resulting in FMF.<sup>3</sup> FMF is rare in non-Mediterranean populations, which might mislead physicians to diagnose inflammatory bowel disease (IBD) in patients who present with the intestinal symptoms of FMF.

Recent studies suggest an association between *MEFV* and IBD,<sup>4</sup> although *MEFV* mutations make no significant contribution to IBD susceptibility.<sup>5</sup> This patient with FMF showed colonic lesions mimicking CD. Despite her refractoriness to conventional IBD treatment, colchicine dramatically relieved her symptoms with the improvement of colonic lesions, and she has had no relapse in the last 2 years. This clinical course and genetic analysis led to a diagnosis of colonic lesions related to FMF. Local circulatory disturbance at colonic wall by sustained inflammation related to FMF might result in mucosal damage. Our case suggests that some patients with FMF might have IBD-like mucosal lesions and physicians should consider genetic analysis and colchicine treatment for patients with indeterminate colitis that

do not respond to conventional IBD treatment.

### **Contributors**

SA, HN, YO, and NU looked after the patient. SA, HN, MM, and TC wrote the report.

Written consent to publish was obtained.

## References

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## Figure Legends

**Figure 1.** Colonoscopic views at the cecum and transverse colon before (A, C) and after (B, D) colchicine treatment.

A: Circumferentially erythematous mucosa with erosions at cecum. B: Remarkable improvement of colonic inflammation with patchy erosions at cecum. C. Pseudopolypoid like lesions at transverse colon. D. Scar formation alone at transverse colon.

**Figure 2.** Genetic analysis for the Mediterranean fever gene mutation. A heterozygous mutation in *MEFV* gene, a 910G>A point mutation, was revealed. This genetic mutation causes a Gly304Arg missense mutation on pyrin. The sequencing number was counted from the head of the primer.