LETTER TO THE EDITOR

Successful Treatment of a Crohn’s Disease Patient Infected with Bacteremic *Mycobacterium Paratuberculosis*

TO THE EDITOR: Antibiotic therapy in the treatment of Crohn’s disease is controversial (1, 2). The profound clinical and colonoscopic response to atypical mycobacterial antibiotic therapy documented in this case establishes that properly chosen antibiotics may be beneficial for some Crohn’s disease patients. The presence and subsequent disappearance of *Mycobacterium paratuberculosis* DNA in the blood from a Crohn’s disease patient associated with complete clinical remission is intriguing.

At the age of 43, this male patient was hospitalized with severe colitis and mouth ulcers. At age 48, the patient was diagnosed with granulomatous colitis; however, the symptoms subsided without specific therapy until age 58, when he re-experienced the same symptoms including the detection of granulomatous colitis and was finally diagnosed with Crohn’s disease for which he received increasing doses of mesalamine, prednisone 60 mg daily, and 6-MP 100 mg daily. At age 61, he developed severe chronic ulcers on his feet and legs that were diagnosed as pyoderma gangrenosum. His symptoms of abdominal cramps, diarrhea, rectal bleeding, fatigue, and weight loss worsened. He had recurrent mouth ulcers for the past 4 yr. His surgical history was positive for bilateral inguinal hernias. He had no other medical problems, and did not smoke nor drink alcohol. He grew up in the Seattle countryside, ate normal diet including dairy products, and has no family history of IBD.

At age 63, this Crohn’s disease patient refused treatment with infliximab because of concern of possible side effects. The result of his colonoscopy was consistent with severe Crohn’s disease, in which the cecum and right colon were severely involved, but skip lesions were found in the transverse, descending, and sigmoid. The rectum appeared normal. Lesions consisted of edema, exudates, cobblestoning, and ulcers (Fig. 1A). The patient consented to give two 4-mL tubes of blood for analyses of the presence of *M. paratuberculosis*, the causative agent of Johne’s disease in cattle and a debated suspect in Crohn’s disease pathogenesis. Circulating leukocytes were analyzed for the presence of *M. paratuberculosis* DNA using nested PCR and nucleotide sequencing (3). As

Figure 1. Colonoscopy healing in a Crohn’s disease patient using antibiotics therapy. (A) represents a colonoscopy image before antibiotics treatment, whereas (B) represents colonoscopy image following 6 months of treatment with split doses of clarithromycin 1,000 mg daily, rifabutin 300–450 mg daily, and levofloxacin 500 mg. (C) represents PCR detection of *M. paratuberculosis* DNA in the blood from a Crohn’s disease patient, whereas *M. paratuberculosis* DNA was detected in the blood before the treatment (lane I-5) and absent in the patient blood after 6 months of treatment (lane II-5). The amplified PCR product on agarose gel in image C is a 298 bp from the IS900 gene of *M. paratuberculosis*. Lane 1 contains molecular weight marker in base pair (bp). Lane 2 contains DNA template from a laboratory strain of *M. paratuberculosis* (positive control). Lanes 3 and 4 represent negative controls (no *M. paratuberculosis* DNA).
shown in Figure 1C, *M. paratuberculosis* DNA is present in the patient’s blood. Consequently, the patient started treatment consisting of split doses of clarithromycin 1,000 mg daily, rifabutin 300–450 mg daily, and levofloxacin 500 mg daily. His treatment with prednisone and 6-MP were slowly discontinued. He experienced fevers and “flu-like” symptoms. Three weeks later, his Crohn’s disease symptoms of abdominal pains, diarrhea, and fatigue disappeared. His appetite returned and he gained 12 lbs over the ensuing months.

He returned for a follow-up visit 6 months later, at which time he was judged to be in total clinical remission from his Crohn’s disease. A colonoscopy was performed that showed no evidence of any active inflammation. There were residual mucosal pseudopolyps in the areas of previous involvement. Importantly, the areas of previous severe involvement in the cecum and ascending colon were normal (Fig. 1B). Blood analysis for the presence of *M. paratuberculosis* DNA was negative in the patients’ blood following treatment (Fig. 1C).

Although showing that one Crohn’s disease patient responds so dramatically to properly chosen antibiotics establishes the concept that antibiotics can be beneficial for some Crohn’s patients, it does not establish that antimycobacterial antibiotics are effective for all patients, nor does it prove that *Mycobacterium* is necessarily one of the causes of the Crohn’s syndrome. Detection of *M. paratuberculosis* fingerprints in the blood of this Crohn’s patient confirms our earlier report (3) and may suggest that a wide spread of this bacterium in our food chain may be alarming. Disappearance of *M. paratuberculosis* in this case study is due to the effective choice of the antibiotics and not because of the anti-inflammatory property of these agents, because the patients did not respond to years of treatment with prednisone.

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REFERENCES