tions of the appendix. The tumor size varied from 2.5 to 60 mm (median: 12 mm), and our case represents the largest appendiceal GIST reported to date. The finding of low mitotic count in this case is consistent with the findings reported by others (3-6). In summary, we document the extremely rare occurrence of appendiceal GIST, increasing the total number of reported cases to nine. To our knowledge, this is the first case with description of tumor size of more than 5 cm.

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To the Editor,
Cardiac involvement is a rare extraintestinal manifestation of inflammatory bowel disease (IBD). However, it can also arise as a secondary effect of drugs containing mainly mesalamine (4,5), which was thought to be a beneficial medication in the treatment of patients with IBD. We herein report a 29-year-old woman with Crohn’s disease (CD) who developed acute myocarditis while receiving per os mesalamine (5-aminosalicylic acid [ASA]). The cardiac complications responded well to the interruption of mesalamine, while the underlying bowel disease responded favorably to corticosteroids and azathioprine administration.

A female patient, aged 29, presented to the emergency department of our hospital because of a sudden syncope and convulsion, accompanied by urinary and fecal incontinence. Seven months previously, she was diagnosed with CD on the basis of endoscopic and histological findings. The first attack of CD was of mild severity and settled promptly with a moderate dose of mesalamine (4.0 g/d per os). With a gradual clinical improvement, the dose of mesalamine was reduced to 2.0 g/d as a maintenance treatment. This treatment was started more than five months prior to her present admission to the hospital. The patient had no other side effects that could be attributed to mesalamine treatment. A physical examination revealed the following: body temperature 36.7°C, blood pressure 88/63 mmHg, and pulse 129 beats/minute. A gallop rhythm was heard. Electrocardiography (ECG) was performed and showed low vol-

Myocarditis due to mesalamine treatment in a patient with Crohn’s disease in China

Crohn hastalığında mesalamin tedavisine bağlı miyokardit

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tage in the limb leads and T wave inversions in leads V2–V6 (Figure 1). A complete blood cell count (CBC) revealed that the number of white blood cells (WBC) had increased to 17,900/μl. Blood chemistry results, namely cardiac troponin I, creatine phosphokinase-MB fraction (CK-MB), creatine phosphokinase (CK), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH) were elevated (1.66 ng/ml, 42 U/L, 392 U/L, 78 U/L, 614 U/L and 9.7 U/L, respectively). Coronary angiography revealed normal coronary vessels. A subsequent echocardiography (ECHO) revealed depressed left ventricular systolic function and global hypokinesis, with a significant reduction in ejection fraction (EF) to 20%–30% (Figure 2). A diagnosis of acute myocarditis was made based on the relevant clinical picture and laboratory results.

As myocarditis was suspected as an adverse reaction associated with the mesalazine treatment, the drug was withdrawn. She was treated with a high dose of intravenous methylprednisolone, which resulted in a gradual clinical improvement. One week later, the ECG showed normal findings, and all the blood chemistry results decreased to normal levels. Repeated ECHO revealed an EF of 66%. The intravenous corticosteroid was then changed to per os prednisone (40 mg/d). The dosage of prednisone was gradually reduced at a rate of 5 mg per week. The corticosteroid was stopped eight weeks later, which caused recurrence of the clinical and laboratory signs of CD. The patient was again admitted to the hospital, and treatment with prednisolone per os was reintroduced. Fortunately, the patient responded very well to the treatment. At the end of the first week, the patient was already in clinical remission. Meanwhile, azathioprine was added at a dose of 1.5 mg/kg/d in order to continue its use after stopping the administration of corticosteroids. One month later, the patient was asked to have routine blood test and liver function test conducted every two weeks, which showed no abnormality.

The administration of azathioprine was continued. Now, after almost one year of treatment with azathioprine, her CD was under control and remained quiescent. The patient has done well since discharge, and no signs of recurrence of either cardiac or small bowel disease are evident.

Cardiac complications have been reported as a rare extraintestinal manifestation of IBD or as a very rare drug reaction to 5-ASA products. Extraintestinal symptoms of IBD usually manifest years after diagnosis, appearing mainly in patients with ulcerative colitis (UC). In our case, the pati-

![Figure 1](image1.png)  
*Figure 1.* Low voltage in the limb leads and T wave inversions in leads V2–V6.

![Figure 2](image2.png)  
*Figure 2.* Echocardiogram view showing depressed left ventricular systolic function and global hypokinesis.
ent developed acute myocarditis seven months after the diagnosis of CD, and no viral prodrome was evident from her history. The symptoms resolved after withdrawal of mesalazine. We thus assume that mesalazine was the causative agent of the myocarditis. A provocation test carried out by administering the potential etiologic agent once more could probably verify the diagnosis, but considering the severe clinical status of the patient and the fatal case of myocarditis reported, this was considered too dangerous.

At present, there is no large-scale epidemiologic data on IBD in the Asia–Pacific region, but several studies have shown an increased incidence and prevalence of IBD in this region (1,2). Compared to the West, there appears to exist a time lag phenomenon. In addition to geographic differences, ethnic differences have been observed in the multiracial Asian countries (3). Moreover, the genetic backgrounds are different in the Asian compared to Western patients (4). Diagnosis of IBD in this region poses special problems. The lack of a gold standard for the diagnosis of IBD and the existence of a variety of infectious enterocolitis with similar manifestations to those of IBD make the differential diagnosis particularly difficult.

On the other hand, with the increasing use of biological therapy, the burden of financial means is set to surge in the Asia–Pacific region. As is reported, in patients who have failed with or are intolerant of immunomodulators, biologic drugs are significantly more effective than placebo at inducing and maintaining remission (5,6). However, this benefit comes with a significant financial cost of up to US$18,000/patient per year for induction and maintenance therapy. The direct and indirect costs of IBD were recently assessed in the Australian population by Access Economics as approximately US$350 million and approximately US$1.5 billion, respectively (7). In most Asia–Pacific countries, biologics are available to only a very small proportion of the population, or not available at all. This issue must be addressed by both health funding agencies and pharmaceutical companies.

In conclusion, the possibility of cardiac involvement, although rare, needs to be considered in patients with CD who are being treated with mesalamine. Clinicians should not only be aware of this potential cardiac complication of IBD but also of the options for therapy. In the Asia–Pacific region, dominated by developing countries, there is a lack of data concerning the use of biological drugs. Because of the relative lack of resources and financial means for IBD treatment in most of the Asian countries, special attention should be given to the cost effectiveness.

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