Pattern of Relapses in Iranian Patients with Ulcerative Colitis. A Prospective Study

Nasser Ebrahimi Daryani, Mohammad Bashashati, Setareh Aram, Ali Asad Hashtroudi, Madjid Shakiba, Alireza Sayyah, Atoosa Nayer-Habibi

Department of Gastroenterology and Hepatology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background. The pattern of relapses in patients with ulcerative colitis (UC) has a significant role in taking decisions about the therapy and the follow up of patients. This study is designed to find out the pattern, time and severity of relapses in Iranian patients with UC. Method. From 1991 to 2003, a period of 13 years, the pattern of relapses in 163 patients with UC who had been admitted to a private referral gastroenterology clinic in Iran were evaluated. Results. 163 patients (58.3% female, 41.7% male) were included, aged from 17 to 74 years with mean age of 38.9 ± 12.3 years. Mean follow up time was 52.7 ± 41.4 months (ranges 12 and 155 months). Mean relapse chance was 0.028 ± 0.036 for each patient in every month (ranges 0-0.21). The mean time from the initial attack to the first relapse was 23.8 ± 22.5 months, which was not the same in patients with different primary disease severity (p=0.03). Conclusion. The time and severity of the relapses relate to the severity of UC. Iranian patients have a milder course of the disease.

Key words
Ulcerative colitis - relapse pattern - Iran

Introduction

Inflammatory bowel disease is a chronic gastrointestinal disease and comprises Crohn’s disease and ulcerative colitis (UC). The latter seems to be more common in Iran (1,2). Ulcerative colitis is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon. It almost invariably involves the rectum and may extend in a proximal and continuous fashion to involve other portions of the colon. Ulcerative colitis is more common in young adults; therefore the patients will handle their disease for a long time. The most important signs and symptoms include bloody diarrhea, mucus passage and tenesmus; but in severe cases constitutional symptoms such as anorexia, weight loss, fever and tachycardia will add to clinical features (3). The course of ulcerative colitis typically consists of intermittent exacerbations alternating with periods of complete asymptomatic remission. A small percentage of patients, however, have continuing symptoms and are unable to achieve remission (4).

Diagnosis is based on endoscopic findings and the pathologic confirmation. The primary end points of therapy should be the induction and maintenance of remission (5). Knowledge of the pattern of relapses has a significant role in making decisions about the therapy and the follow up of patients. This study is designed to find out the pattern, time and severity of relapses in Iranian patients with UC.

Method

This study is a prospective descriptive investigation. It was conducted by Tehran University of Medical Sciences, and was approved by the Ethics Committee of this university. A questionnaire which was a part of our UC registration form, was completed for patients with definite diagnosis of UC based on clinical features, endoscopic and pathologic findings, who had been admitted to a private referral gastroenterology clinic in Tehran, Iran. From 1991 to 2003, 465 patients with UC were referred to our clinic. Because of the long period of this study and the chronic evolution of the disease, some patients referred rarely; thus information of patients who were referred at least one year and followed up at least 75% of the visit dates were processed. Moreover, we did not include patients who had been referred during the chronic phase of their diseases, and not at their initial attack phase. Finally, 163 patients were enrolled in this study.

The severity of the initial attack and of the relapses were defined according to the criteria of Truelove and Witts (6).
The medical treatment protocol for our patients consisted of 5-ASA agents for mild to moderate UC and glucocorticoids for moderate to severe UC. In mild forms if we did not obtain the acceptable response we used glucocorticoids. For steroid-refractory and steroid-dependent forms we administered azathioprine. Maintenance therapy consisted of 5-ASA or azathioprine according to the active phase treatment.

Visit dates were determined based on the patient’s condition; if the patient was in remission or relapse, he was referred every 3 months or monthly, respectively. Patients were told to refer immediately if they had any new problems or relapses. On each visit the questionnaire was completed by a general physician, and then the patient was seen by a specialist. If the patients complained of any extra intestinal symptoms, they were referred to a specialist (e.g. ophthalmologist or rheumatologist) and if confirmed, it was documented as an extra intestinal manifestation.

Survival analysis of the time between the initial attack and the first relapsing phase, and also of the severity of the initial attack as a predictor of relapses, was made. The hypothesis that the severity of the initial attack correlates with the period of time up to the first relapse was studied. The Kruskal Walis test was also done.

Results

One hundred sixty three patients (58.3% female, 41.7% male) were included, aged from 17 to 74 years with mean age of 38.9 ± 12.3 years. Mean follow up time was 52.7 ± 41.4 months (ranges: 12 to 155 months). During the initial attack, the disease extension was registered for 151 patients, and the involvement of different parts of the colon was the following: rectum in 31 cases (20.5%), sigmoid in 24 cases (15.9%), descending colon in 51 cases (33.8%), hepatic flexure in 22 cases (14.6%), and pancolitis in 23 cases (15.2%). Disease severity was determined on the initial attack for 139 patients; of them, 48 cases were mild (34.5%), 49 cases moderate (35.3%) and 42 cases were severe (30.2%).

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In patients with moderate disease severity, relapse occurred significantly later than in those with mild or severe disease (Log rank test, p=0.002) (Fig.1). We categorized the patients into two groups, mild and severe (those with mild and moderate disease were placed into group mild and those
with severe disease into group severe); those with mild disease had a mean time of 31±4 months up to first relapse (95% CI=23-40), and median of 22 months (95% CI=16-28); those with severe disease had a mean time of 19±2.5 months and median of 13 months (95% CI=9-17) (p=0.0076) (Fig.2).

Out of the patients who received azathioprine, 8 patients (15.09 percent) relapsed. Six patients out of these improved (75%) and only two patients underwent colectomy. It is notable that two patients (2.4%) had undergone colectomy before administration of cyclosporine.

Colonoscopy was repeated in 44 patients. Thirteen of them had either an uncertain primary diagnosis or no primary evaluation of the disease extension. Other patients had undergone colonoscopy for the colitis surveillance. The extension of involvement was as follow: in 5 patients (11.3%) up to rectum, in 3 patients (6.8%) up to sigmoid, in 16 patients (36.3%) up to descending colon, in 4 patients (9%) up to hepatic flexure, in 12 patients (27.2%) pan colitis and in 4 patients (9%) was normal. Extension of involvement had no significant statistical difference between the first and second colonoscopy.

Discussion

The course and prognosis of UC are often reported in terms of mortality (7), morbidity (4) and cancer risk (8). Some studies have assessed the relation between the time from diagnosis and disease activity, showing some factors predicting the clinical remission of colitis (9).

Changes in the morbidity pattern of ulcerative colitis have created a need to update the understanding of the course of the disease (10). In this study, we assessed the severity of the first manifestation and also the following relapses in 163 Iranian patients with UC which is the most common form of inflammatory bowel disease in Iran.

According to the literature, a few patients with UC may present with a single initial attack without any relapses. Stewenius et al, during a ten years follow up, reported the relapse rate about 70% (10). This is compatible with our results that showed 63.8% of patients experienced at least one episode of relapse after a 13-year follow-up. The high rate of no relapse during the follow up period, gave some concern about the definite diagnosis of UC. Therefore we checked our patients’ registries, during the years out of the study period (2003 to 2006). We found out that 23 patients remained on remission phase, and 36 patients experienced their 1st relapse during these years. Median time between their initial attack and 1st relapse was 26 months (range: 12-160 months), mainly related to drug discontinuing. It seems that in Iranian patients the course of UC is milder; it is in concordance with another report from Iran, which was published about 20 years before (2).

Moreover, five of those with no relapses had simultaneous primary sclerosing cholangitis (PSC). In our previous report, we showed that development of PSC in patients with UC might have a positive effect on colonic disease (9).

The extent of the disease in the colon is also an important prognostic factor. Patients with distal colitis show a lesser tendency to relapse (11). Relapse in our patients with disease confined to splenic flexure occurred significantly later than in others. The clinical course in such patients is usually benign. It could be compatible with previous studies, which revealed that in 20% of such patients the disease resolved spontaneously (12).

One study suggested that the risk of relapse increased in younger patients (aged 20 to 30), in women, those with more than five prior relapses, and those with basal plasmacytosis on rectal biopsy specimens (13). In one report, young patients (less than 20 years) and older patients (over 70 years) had a higher relapse rate and were more likely to suffer a severe attack than patients between the ages of 20 and 70 (14). On the other hand, analysis of relapses’ interval showed that one relapse reduces the interval between the following relapses.

In accordance to survival analysis, 50% of relapses occurred during the first 15 months. It is notable that if a patient had no relapse during the first 5 years, the chance of reactivation of the disease was only 10%. Therefore avoiding the risk factors that trigger activation of the disease is an important factor in preventing relapses (15). Follow up of patient and correct usage of drug regimen during the first five years are also very important.
This study has some limitations. We attempted to validate the information in patient profiles with additional questionnaires and detailed interviews. Memory imperfections, especially in this long period and with the pattern of the chronic disease, are notable (9).

It can be concluded that the time and the severity of relapses are associated with the severity of UC. Moreover, the course of UC is milder among Iranian patients. Complementary studies on environmental and biologic relative factors are recommended in our region.

References