Ulcerative Colitis in Thailand: A Clinical Study and Long Term Follow-up

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Abstract

Ulcerative colitis (UC) is uncommon in Thailand. Few reports have been published and confirmation of the diagnosis was difficult. To make a firm diagnosis of UC in Thailand, long-term follow-up and demonstration of chronic and relapsing clinical courses should help to confirm the existence of UC in Thailand.

Objective: To review the demographic data, clinical presentation and clinical courses of the diagnosed UC cases in Thailand.

Material and Method: Diagnosed UC patients who were followed-up for longer than 3 months at the Diarrhea Clinic, Siriraj Hospital between 1988-2000 were included.

Results: Forty cases of UC were followed-up. The duration of follow-up ranged from 3-75 months (mean 27 months). Male to female ratio was 19:21 and age of onset varied from 13-77 years (mean 37.7 years). Extents of the disease was left-sided colitis in 58 per cent, left and right-sided colitis in 8 per cent, pancolitis in 21 per cent, proctosigmoiditis in 13 per cent and ileal involvement in 8 per cent. At presentation, the disease was mild in 28 per cent, moderate in 60 per cent, severe in 13 per cent and fulminant in 2. Clinical presentations were diarrhea in 97.5 per cent, lower GI bleeding in 17.5 per cent, abdominal pain in 50 per cent, fever in 27.5 per cent, weight loss in 62.5 per cent and extraintestinal manifestations in 20 per cent. Diagnoses were made in all cases by sigmoidoscopy plus barium enema or colonoscopy and biopsies were taken in all cases. Histologic findings supported the diagnoses in 69 per cent of cases. Seventy per cent responded to sulfasalazine or 5-ASA with or without corticosteroid, but in 30 per cent, azathioprine was added for a period during the treatment. Clinical courses of the diseases were chronic intermittent with remission and relapse in 44 per cent, chronic continuous activity without remission in 27 per cent, single episode without relapse in 27 per cent and acute fulminating course in 6 per cent. One patient died from fulminant pancolitis with colonic perforation. There was no colonic cancer in our cases throughout the follow-up period.

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Conclusions : UC is very uncommon in Thailand. Firm diagnosis of UC can be made through long-term follow-up and demonstration of chronic and relapsing clinical courses. The disease severity and extent of disease involvement was slightly different from that in Western countries. Incidence of extraintestinal manifestation was 20 per cent. Most cases responded to sulfasalazine, 5-ASA or corticosteroids.

Key word : Ulcerative Colitis, Inflammatory Bowel Disease, Colitis, Diarrhea, Clinical Course, Thailand

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Ulcerative colitis (UC) is a chronic inflammatory disease of unknown etiology involving the colon. The disease is more prevalent in the Western countries and was considered very uncommon among Asian countries including Thailand. So far, there have been only a few reports of UC cases in Thailand and none reported long term follow-up results to confirm the chronic and relapsing clinical course of UC[1-3]. Whether there is any difference in the clinical features of UC in Thailand from that in the Western countries, is not known. Infectious colitis in Thailand is very common and there is often confusion in the diagnosis of infectious colitis and UC. Histologic findings can sometimes be helpful in differentiating infectious colitis from UC, but this is not always true. Most infectious colitis usually resolves with specific treatment if the infectious agents are found. Ulcerative colitis usually has a prolonged clinical course and frequently relapses or recurs with or without precipitating factors. Response to sulfasalazine or 5-aminosalicylic acid (5-ASA) and/or corticosteroids or azathioprine (AZA) together with the demonstration of a prolonged and relapsing clinical course should help to make the diagnosis of UC easier to establish. The objective of this study was to review the clinical spectrum and clinical courses of the diagnosed UC cases in the Diarrhea Clinic, Siriraj Hospital, Thailand. The long-term follow-up of the cases presented in this study should help establish the existence of UC in Thailand.

MATERIAL AND METHOD

Forty patients who were diagnosed with UC and followed-up for at least 3 months at the Diarrhea Clinic of Siriraj Hospital, Bangkok, Thailand from 1988 to 2000 were included. Clinical and demographic datas were retrospectively reviewed.

Diagnosis of UC: The diagnosis of UC in all cases was based on; 1) history of diarrhea, either mucus bloody, watery, semisolid or frank bleeding per rectum, that was not controlled by adequate antibiotics against pathogenic enteric bacteria and by metronidazole against amoebic colitis 2) negative stool examination for amoebic trophozoites and other parasites, together with negative culture for pathogenic bacteria 3) compatible sigmoidoscopic or colonoscopic findings and/or compatible distribution of colitis shown in barium enema examination 4) suggestive histologic features (e.g. decrease and distortion of glandular structures, chronic inflammation limited to the mucosa, crypt abscesses, etc.) shown from colonic or rectal biopsies 5) clinical course of the disease longer than 3 months 6) response to sulfasalazine/5-ASA or corticosteroids.

Extent of disease: Extent of disease involvement as assessed by colonoscopy or barium enema was classified as: 1) *proctosigmoiditis* : involvement up to rectum or sigmoid colon 2) *left-sided colitis* : involvement up to descending colon or splenic flexure 3) *left and right-sided colitis* : involvement up to transverse colon or hepatic flexure 4) *pancolitis* : involvement of the whole colon up to

caecum 5) *Backwash ileitis:*involvement of caecum and terminal ileum.

Severity of disease: Severity of the disease was classified according to Truelove and Witts' classification[4].

Clinical course of disease: The clinical course was classified into 4 categories: 1) a single episode without relapse. 2) a chronic intermittent course with remission and relapse. 3) a chronic continuous course without complete remission 4) acute fulminating course with life threatening conditions e.g. massive lower gastrointestinal bleeding, toxic megacolon or colonic perforation.

In all cases, colonic cancer was suspected if there were unexplained anorexia, weight loss or lower gastrointestinal bleeding which were unresponsive to corticosteroids or azathioprine. Barium enema and/or colonoscopy would be performed to confirm or exclude colonic cancer.

Test of p-ANCA: Standard indirect immunofluorescence (IIF) method was used to detect ANCA. Sera samples were considered negative if specific neutrophil staining was equivalent to or less than the negative control. A sample was considered positive if cytoplasmic or perinuclear staining was observed. On ethanol fixed slides, if the samples showed predominant perinuclear pattern, they were considered p-ANCA positive.

RESULTS

Overall, there were 40 cases of UC during the 12-year-period. Nineteen patients were male and 21 were female. Mean duration of follow-up varied from 3 to 75 months with an average of 27 months. The distribution of age at onset of the disease was shown in Fig. 1, and the mean age of onset was 37.7 years.

Extent of disease involvement was evaluable in 38 patients (Table 1). Left-sided colitis was found in 22 patients (58%), left and right-sided colitis in 3 (8%), pancolitis in 8 (21%), proctosigmoiditis in 5 (13%) and ileal involvement (backwash ileitis) in 3 (8%), All patients with ileal involvement were in the pancolitis group.

Severity of the disease

At presentation, severity of the disease was classified as mild in 11 of 40 patients (27.5%), moderate in 24 (60%), severe in 3 (7.5%) and fulminant in 2 cases (5%). Among the 2 fulminant cases, one had colonic perforation and the other had

Table 1. Extent of disease involvement in 38 ulcerative colitis patients.

	No. of patient	%
Proctosigmoiditis	5/38	13
Left-sided colitis	22/38	58
Left and right-sided colitis (up to hepatic flexure)	3/38	8
Pancolitis	8/38	21
Ileitis	3/38	8

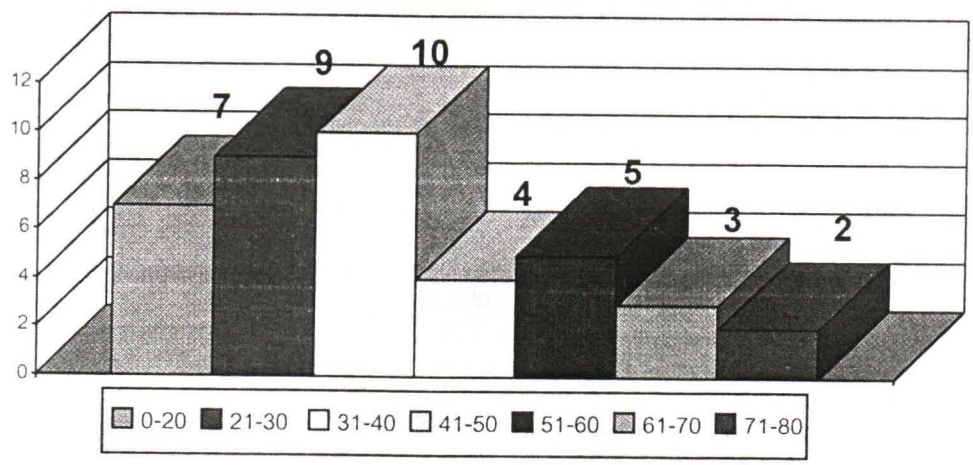

Fig. 1. Distribution of age at the onset of ulcerative colitis in 40 patients.

Table 2. Clinical presentations of 40 ulcerative colitis patients.

	Number	%
Diarrhea	39	97.5
Lower GI bleeding	7	17.5
Abdominal pain	20	50
Tenesmus	16	40
Fever	11	27.5
Weight loss	25	62.5
Extraintestinal manifestations	8	20
Oral ulcer	2	5
Conjunctivitis/keratitis/uveitis	3	7.5
Polyarthritis	2	5
Ankylosing spondylitis	1	2.5
Sclerosing cholangitis	1	2.5

Table 3. Diagnostic methods performed in 40 ulcerative colitis patients.

	Number abnormal per number performed	%
Stool exam	20/22	91
Barium enema	23/28	82
Sigmoidoscopy	25/27	93
Colonoscopy	23/23	100
Histology	24/35	69
p-ANCA	12/32	37.5

p-ANCA = Perinuclear Antineutrothil Cytoplasmic Antibodies

massive lower gastrointestinal bleeding. Both patients underwent emergency surgery without total colectomy.

Clinical Presentation

Clinical presentation of UC was shown in Table 2. The most common clinical presentation was diarrhea (watery, semisolid or mucus-bloody), which was found in 39 of 40 patients (97.5%). One patient who did not present with diarrhea, had fever of unknown origin and diarrhea developed 6 months later. Lower gastrointestinal bleeding was found in 7 patients (17.5%). Most bleeding was not severe except for the one patient who had massive bleeding which later required emergency surgery. Abdominal pain was found in 20 cases (50%) and tenesmus in 16 (40%). Fever was found in 11 (27.5%) and weight loss in 25 patients (62.5%). Eight patients (20%) had extraintestinal manifestations, which included aphthous ulcers in 2, conjunctivitis, keratitis and uveitis in 3, polyarthritis in 2, ankylosing spondylitis in 1 and sclerosing cholangitis in 1.

Diagnostic Methods (Table 3)

Stool examination revealed numerous WBC and RBC in 91 per cent of the cases. Barium enema showed features of 'colitis' compatible with UC in 82 per cent. Sigmoidoscopy showed variable severity of colitis in almost all cases (25/27, 93%). However, there were 2 patients with negative initial sigmoidoscopic finding but subsequent colonoscopy showed colitis at the rectosigmoid region. Positive findings were found in all cases who underwent colonoscopy (100%). Histologic features showed sufficient evidence to diagnose UC with certainty in 69 per cent, the rest (31%) was designated as 'non-specific acute or chronic colitis'. Serology for p-ANCA assay was performed in 32 patients and was positive in 12 (37.5%) cases.

Treatments

Twenty-eight patients (70%) responded to sulfasalazine or mesalamine with or without corticosteroids. Azathioprine (50-100 mg/day) was administered in twelve patients (30%) who either could not tolerate the adverse effects of corticosteroids, or were steroid-dependent or steroid unresponsive. Laparotomies were performed in 3 cases, 2 of which had fulminant colitis (one had colonic perforation and the other had massive lower gastrointestinal bleeding). Colostomy without total colectomy was performed in 2 cases. One case had severe relapse of pancolitis with rectal perforation. He later had total colectomy but finally died of sepsis.

Clinical course

The clinical course of disease was evaluable in 33 patients. Seven patients with a clinical course of the disease less than 6 months were not in-

Table 4. Clinical courses of the 33 ulcerative colitis patients.

	Number	%
Chronic intermittent course	15/33	44
Chronic continuous activity	9/33	27
Single episode without relapse	9/33	27
Acute fulminating course	2/33	6

cluded, as it may be too short to observe the clinical progression of the disease. The total duration of their clinical courses varied from 6 to 168 months with the mean of 50 months. The clinical course of 33 patients is shown in Table 4; chronic intermittent with remission and relapse in 15 (44%), chronic continuous activity without remission in 9 (27%), a single episode without relapse in 9 (27%) and acute fulminating course in 2 (6%). One patient who initially presented with severe proctitis was later progressed to pancolitis and died from colonic perforation during the disease relapse. No colonic cancer was detected during the period of follow-up.

DISCUSSION

Ulcerative colitis is a common disease in Western countries. It is considered uncommon in Asian countries, including Thailand. So far, there were only few reports of UC in Thailand[1-3]. Viranuvatti et al, reported the largest series which included 93 patients. However, there was no long-term follow-up and the possibility of infectious colitis could not be firmly excluded[3]. In the present study, the 40 diagnosed UC cases were regularly followed-up at the Diarrhea Clinic, Siriraj University Hospital for 3-75 months (mean 27 months) during the 12-year-period. The prolonged clinical courses with intermittent remission and relapse as shown in this study, made the possibility of infectious colitis highly unlikely. The response to sulfasalazine/ 5-ASA and corticosteroids or azathioprine, without specific antimicrobial therapy for infectious colitis should firmly exclude infectious colitis.

The slightly female preponderance (female to male ratio 21:19) as shown in this study was comparable with other studies from Western and Asian countries. The mean age of onset of the disease was 37.7 years. In Western countries there are bimodal peak of age of onset, which usually ranges from 15-30 and 55-65 years old[5].

The extent of the disease involvement in the present study was predominantly left-sided colitis (58%) and proctosigmoiditis in 13 per cent, while in other studies, rectosigmoiditis (44-49%) was more common than left-sided colitis (36-41%)[6]. The incidence of pancolitis was 21 per cent in the present study. This was also comparable to 14-36.7 per cent in other series[6].

Early report by Edwards and Truelove showed that majority of cases was mild in 54 per cent, while 27 per cent was moderate and 19 per cent severe[7]. In the present study, the majority of cases was moderate (60%), and mild in 27.5 per cent, severe in 12.5 per cent. In general, the greater anatomic extent of disease involvement at first presentation, the more likely the severity of disease[8]. However, Langholz et al, reported moderate disease severity of UC in 70.7 per cent of cases, mild in 20.2 per cent and severe in 9.1 per cent[9].

Diarrhea, abdominal pain, tenesmus and weight losses were the most common presentations, which is similar to most studies[10]. In general, extraintestinal manifestations are present in fewer than 10 per cent of cases at initial presentation[10]. In the present study, extraintestinal manifestation was found in 20 per cent of cases at some time during the course of illness.

In general, UC can be firmly diagnosed by compatible clinical features and exclusion of other causes of colitis (especially infectious colitis). In the present study, sigmoidoscopy and colonoscopy showed evidence of colitis in 93 per cent and 100 per cent of cases respectively, which should serve as useful tools in diagnosing UC. Barium enema was normal in 18 per cent of the patients in the present study especially in patients with mild colitis. Loose et al, found normal barium enema in 14 per cent of their cases with pancolitis[11]. However, barium enema together with sigmoidoscopy is superior to barium enema alone in diagnosing UC.

Histologic features can be very suggestive of UC but can never be characteristic or pathognomonic. Crypt abscesses can also be found in many infectious colitides. Other histologic features which were reported as helpful in diagnosing UC were : 1) evidence of chronic colitis with the presence of lymphoid aggregation, infiltration in lamina propria with plasma cells, mast cells, or eosinophils, 2) distortion of crypt architecture including reduction in number, shortening and branching of the crypt glands. In general, these features can usually distinguish infectious colitis from UC with an accuracy of 80 per cent[12,13].

Most acute self-limited and infectious colitis usually last no longer than a few weeks. Shigellosis seldom lasts more than 4 weeks[14,15]. Campylobacter colitis, antibiotic-associated colitis might last up to 2 months, if left untreated[16-19]. Amoebic colitis, without proper treatment, often progresses to severe colitis, toxic megacolon, abscess

or perforation if left for many months[20,21]. Hence, the duration of colitis may be helpful in differentiating UC from other colitis, especially if longer than 3-6 months. In the present study, the duration of colitis in all cases was longer than 3 months before they were included in the study. This made it highly unlikely to be infectious colitis. When coupled with long term follow-up, which showed a recurrent and relapsing clinical course in most cases, the diagnosis of UC was very convincing. Response to sulfasalazine and corticosteroids or azathioprine was also very helpful in confirming the presence of UC in Thailand. Sulfasalazine and corticosteroids were successful in inducing remission in 70 per cent of the cases in this study, while the rest needed additional azathioprine.

In the present study, nearly half of the cases had a chronic intermittent clinical course. A quarter had a chronic continuous course without relapse. Acute fulminant colitis was found in 6 per cent of the cases. Edwards and Truelove found a chronic intermittent course in 64.4 per cent, a chronic continuous course in 7.2 per cent, a single episode of colitis in 18 per cent and an acute fulminating course in 0.8 per cent[7]. The variability of the clinical course from one study to another could be due to the variability of management strategies in each study. There was no correlation between the age of onset, extent of the disease or disease severity with the types of clinical course in the present study.

One of the presented cases who had had UC for over 10 years recently had exacerbation and follow-up colonoscopy showed 2 cm polyps at transverse colon. After polypectomy, the histology showed an adenomatous polyp without metaplasia. No colonic cancer was found in the present series.

SUMMARY

UC is very uncommon in Thailand. The difficulty in making the diagnosis with certainty can be very hard, especially when histologic findings are not characteristic and pathognomonic for UC. Exclusion of acute self-limited and infectious colitis can never be done with confidence. Long-term follow-up is needed to make a firm diagnosis of UC in a country where UC is so uncommon. The extent of disease involvement and disease severity in the presented cases was slightly different from that of Western populations. Left-sided colitis was slightly preponderant in the present series, rather than proctosigmoiditis. Patients with moderate severity of disease were more common than mild and severe forms of disease. The finding of a chronic and relapsing course of disease was an important criteria to exclude acute self-limited and infectious colitis, as well as the response to sulfasalazine, ASA or corticosteroid. The present study proved the existence of UC cases in Thailand and careful surveillance for this difficult to diagnose disease is important and should be carried out through long-term follow-up.

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ภาวะลำไส้ใหญ่อักเสบเรื้อรังในประเทศไทย: ลักษณะทางคลินิกและการติดตามผู้ป่วยระยะยาว

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ภาวะลำไส้ใหญ่อักเสบเรื้อรังพบไม่บ่อยในประเทศไทย เนื่องจากการยืนยันการวินิจฉัยและแยกจากภาวะลำไส้อักเสบจากติดเชื้อทำได้ยาก การติดตามผู้ป่วยระยะยาวและพบลักษณะของโรคที่เรื้อรังและมีการกำเริบเป็นระยะ น่าจะเป็นการยืนยันการวินิจฉัยภาวะนี้ได้ดีที่สุด การศึกษานี้ได้ทบทวนลักษณะทางคลินิกและการดำเนินโรคของผู้ป่วยลำไส้ใหญ่อักเสบเรื้อรัง 40 ราย ที่คลินิกโรคท้องร่วงโรงพยาบาลศิริราช ตั้งแต่ พ.ศ. 2531–2543 เป็นผู้ป่วยชาย 19 ราย หญิง 21 ราย อายุที่เริ่มเป็น 13–77 ปี (เฉลี่ย 37.7 ปี) ระยะเวลาที่ติดตาม 3–75 เดือน (เฉลี่ย 27 เดือน) ผู้ป่วยร้อยละ 58 เป็นที่ลำไส้ใหญ่ด้านซ้าย ร้อยละ 8 เป็นทั้งด้านซ้ายและขวา ร้อยละ 21 เป็นตลอดลำไส้ใหญ่ ร้อยละ 13 เป็นที่ลำไส้ส่วนซิกมอยด์และทวารหนัก และร้อยละ 8 เป็นที่ลำไส้เล็กอิเลี่ยมร่วมด้วย ความรุนแรงของโรค ร้อยละ 28 มีความรุนแรงน้อย ร้อยละ 60 รุนแรงปานกลาง ร้อยละ 13 รุนแรงมาก และร้อยละ 6 รุนแรงมากจนต้องได้รับการผ่าตัดตั้งแต่แรก อาการแสดง ร้อยละ 97.5 ท้องเสีย ร้อยละ 17.5 ถ่ายอุจจาระเป็นเลือดสด ร้อยละ 50 มีอาการปวดท้อง ร้อยละ 27.5 มีไข้ ร้อยละ 62.5 น้ำหนักลด และร้อยละ 20 มีอาการแสดงนอกลำไส้ ทุกรายสามารถให้การวินิจฉัยได้จากอาการ การส่องกล้องตรวจลำไส้ส่วนปลายร่วมกับการตรวจแบเรี่ยม หรือการส่องกล้องตรวจลำไส้ใหญ่ การตรวจทางพยาธิวิทยาสามารถสนับสนุนการวินิจฉัยได้ในร้อยละ 69 ของผู้ป่วย ร้อยละ 70 ของผู้ป่วยตอบสนองดีต่อยาซัลฟาซาลาซีนและคอร์ติโคสเตียรอยด์ ในขณะที่ร้อยละ 30 ต้องได้ยาอะซาไธโอปรีนร่วมด้วย ผู้ป่วยร้อยละ 44 มีการกำเริบเป็นช่วง ๆ ร้อยละ 27 มีการกำเริบตลอดเวลาโดยไม่มีช่วงที่โรคสงบ ร้อยละ 27 มีการกำเริบเพียงครั้งเดียว และร้อยละ 6 โรคมีความรุนแรงมากจนต้องได้รับการผ่าตัดตั้งแต่แรก มีผู้ป่วยเสียชีวิต 1 รายจากภาวะลำไส้ใหญ่ทะลุระหว่างที่โรคกำเริบ แต่ไม่มีผู้ป่วยใดเกิดมะเร็งลำไส้ในช่วงที่ติดตามผู้ป่วย

สรุป : ภาวะลำไส้ใหญ่อักเสบเรื้อรังพบได้น้อยในประเทศไทย การดำเนินโรคมีแนวโน้มจะมีความรุนแรงและกว้างขวางมากกว่าในต่างประเทศ การติดตามผู้ป่วยระยะยาวและพบลักษณะโรคที่เรื้อรังและมีการกำเริบเป็นระยะ ๆ น่าจะเป็นการยืนยันการวินิจฉัยภาวะลำไส้ใหญ่อักเสบเรื้อรังและแยกจากภาวะลำไส้อักเสบจากติดเชื้อที่ดีที่สุด

คำสำคัญ : ลำไส้อักเสบเรื้อรัง, ลำไส้อักเสบ, ท้องร่วง, ลักษณะทางคลินิก

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