Research Paper

Medical Science



Extension of Distal Ulcerative Colitis Over Time

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Abstract

Aim: to evaluate the extension of the inflammatory lesions in patients diagnosed with initial distal ulcerative colitis (UC) and to identify the risk factors associated with the extension.

Methods: The extension of the inflammatory lesions was appraised in 183 patients with ulcerative colitis (UC). Each patient from study group was reexamined on a yearly basis or in the case of a new UC attack. Results: During the period 2000 – 2006 the extension of the disease was observed in 57 (31%) patients (39/103 (37,8) patients with proctitis and 18/80 (22.5%) cases with left colitis) after a mean time of 4.5 years. The risk factors for the expansion of the lesions were intermittent simptoms, age, ex-smokers, extraintestinal manifestations and without maintenance therapy. Conclusions: Progression towards extended colitis was recorded both in patients with proctitis and left colitis but with significant differences as to the average period of time of evolution of the pancolitis.

Keywords: ulcerative colitis, extension, proctitis, left colitis, risk factors

Introduction

In the developmental history of the ulcerative colitis (UC) a series of characteristics (such as the severity of the activity attack, the extension of the lesions and the age of the beginning) confer to the disease certain developmental and prognostic particularities. In the long term follow-up studies, 40% to 70% of the patients with distal UC present a tendency towards extension of the inflammatory lesions (i.e. proctitis and left colitis). The proximal extension of the ulcerative proctitis is frequent and occurs rather late with respect to the initial diagnosis, while the risk of extension of the left colitis after the splenic flexure seems to be lower. Moreover, the patients that present extension of the inflammatory lesions develop more severe forms of the disease more often and have an increased risk for local and general complications

The aim of the study was to evaluate the extension over time of the inflammatory lesions in patients diagnosed with initial distal UC and to identify the risk factors associated with the extension.

Method

The proximal extension of the disease was assessed in 183 patients with distal UC at the moment of the diagnosis (103 with proctitis – 54% females, 46% males, and 80 with left colitis – 45% females and 55% males) who met the following criteria:

- 1. UC diagnosis according to the standard criteria (clinical, endoscopic, radiologic and histologic).
- An initial evaluation of the extension of the disease and of the development course through clinical, endoscopic, radiologic and histological exams.
- 3. Reevaluation of the inflammatory lesions every year or in the instance of a new activity attack.
- 4. Follow-up over a period of 6 years, with an average duration of the disease of 10.64 years.

Personal information, initial extension of the disease, clinico-evolutive pattern and treatment were gathered from the medical history. The time of the diagnosis was defined as the moment of representation of the inflammatory lesions, confirmed as UC by the histological exam. Extension of the disease was defined as proctitis (rectal involvement), left colitis (involvement until the splenic flexure) and pancolitis (involvement of the entire colon).

The distal form was defined on the basis of the follow-up data and colonoscopic investigation of the inflammation, being extended on a macroscopic area of 15 cm in the case of proctitis, or until the proximity of the splenic flexure in left colitis, respectively. The follow-up period of 6 years (a minimum of 24 months) represents the period of observation for the incident cases but also of the cases diagnosed with ulcerative colitis before the year 2000, classified as distal colitis. Each patient was reexamined on a yearly basis or in the case of a new UC attack. The statistical analysis was performed through the Fisher test, p <0.05, efficiency test, t-Student, CI and RR.

Results In the follow-up period, the extension of the disease was recorded in 57 (31%) patients. From 103 patients with initial proctitis, the colitis progressed in 39 patients (37.8%; 20 patients (51,28%) presented left colitis, 12 patients (30,76%) extended colitis and pancolitis in 7 patients (17,94%). From the 80 cases of left colitis, 18 (22.5%) presented extension of the inflammatory lesions classified as pancolitis. It is worth noticing that the extension of the disease by the involvement of a new colon segment can be observed at an average time interval of 4.5 years (predictive value positive for the extension of 56% with a 64% specificity), with the mention that, from the statistical point of view, there is an important difference of the average value expressed in years between the evolution of the proctitis towards pancolitis (15.8 years) and the evolution of the left colitis towards pancolitis (4.43 years) (t-Student = 3.37, GL = 28; p = 0.0027). The relative risk for extension is 1.75 for proctitis and 2.08 for left colitis (table 1).

Table 1. The relative risk for extension for distal OC				
Extension I cases	Extension II* cases	Type of extension cases	Extension time (years)	
Proctitis - 103 (56,28%)	39 (37.8%)	Left colitis – 20 (51.28%)	4.67 ± 5.3	
	RR= 1.75	Extended colitis – 12 (30.76%)	10.13 ± 10.3	
	(c ² 12.32, p= 0.0004 IC 1.33 - 2.31)	Pancolitis – 7 (17.94%)	15.83 ± 11.2	
Left colitis - 80 (43,72%)	18 (22.5%)			
	RR= 2.08	Pancolitis - 18 (22,5%)	4.43 ± 4.2	
	(c ² =10.86, p= 0.0009 IC = 1.32-3.27)			

*t-Student = 3.37, GL = 28; p = 0.0027 RR- relative risk

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The correlations between the extension of the lesions and a series of parameters such as medical history, clinical, endoscopic and therapeutic aspects highlight a statistically significant direct causality ratio (table 2). Proximal progression was more frequently observed in the patients of a young age at the beginning of the disease (n = 25 patients, average age 27.1 ± 31.7) (p = 0.003) and in the 34 patients ex-smokers (11.4% χ² 15.42, RR= 1.81, IC= 1.32-2.48, p= 0.00009). The clinical evolution with continuous and recurrent symptoms was recorded for 10 (17,54%) and 43 patients, respectively (76.59%) (x2 = 19.34; GL = 1; p = 0.00001). An important correlation is also the association between symptoms, mainly between rectal bleeding and the extension of the lesions, with a RR = 3.16 observed in 21 patients (37%) with important rectal bleeding. The presence of extraintestinal manifestations recorded for 8 patients (12.7%) was associated with the poorer evolution of UC (p = 0.005). The extension of inflammatory lesions was recorded in 39 patients (52.63%) who did not follow a systematic maintenance therapy (sulfasalazine or mesalazine), as well as in patients who needed corticotherapy (19.21%) (p = 0.004) (table 2).

Table 2. Univariate analysis of the risk factors for the expansion of the lesions in patients with proctitis and left colitis

Risk factor	Patients with extension of lesion n=57 (31%)	Patients without extension of lesion n= 126 (69%)	Statistic significance
Male gender	34 (60%)	81 (64.4%)	0.38
Age at the time of the diagnosis	27.1 ± 31.7	34.8 ± 5.4	0.13
Extraintestinal manifestations	8 (12.7%)	6 (4,76%)	0.005
Current smoker vs ex-smoker	7 (11.4%) vs 34 (59.64%)	74 (58.7%) vs 13 (10,31)	0.00009
Appendectomy	10 (16.9%)	58 (46%)	0.004
Rectal bleeding	21 (37%)	8 (6.34%)	< 0.001
Chronic activity	10 (17,54%)	6 (5.08%)	0.005
Intermittent activity	43 (76.59%)	96 (76.59%)	0.00001
ASA (free) PDN (needed)	39 (52.63%) 10 (19.21 %)	9 (2.7%) 35 (28.24%)	0.004

Discussions In UC the essential characteristic of the inflammatory process resides in the continuity of the inflammatory lesions which present various intensity degrees throughout the colon. The rectal involvement is mandatory and the passage from the damaged mucosa to the normal is usually abrupt. A particularity is represented by the proximal extension in time of the inflammatory lesions for the patients with initial distal colonic involvement. The extension risk of the lesions is recorded differently in the literature. Meucci et al. investigated the risk of extension at 5 and 10 years after the diagnosis of proctitis. At an average follow-up interval of 52 months, they observed that 27.1% cases presented proximal extension of the lesions, from which one third were pancolites, one fifth - left colites and one tenth had proctites which had to be operated in the 5 years following the diagnosis (1). Farmer reports that after 5 years from the UC diagnosis approximately 5% of the patients with proctitis and 20% of the left colitis patients will display proximal extension of the inflammatory lesions (2). Alkim et al. describe on a series of 193 patients with distal colitis the expansion of the inflammatory lesions in 13.9% cases after an average interval of 3.9 ± 2.9 years (range: 0.8-12) (3).

In our study the extension of the inflammatory lesions was observed in 31% of the patients with initial distal UC, strong differences being recorded between proctitis and left colitis (15.8 versus 4.43) in the average values expressed in evolution years towards pancolitis. After an average interval of 4.5 years, 2 out of 3 patients with proctitis and 2 out of 7 patients with left colitis, respectively, will present involvement of a new colon segment.

From the evaluation of the extension of inflammatory process in patients who presented lesions initially only in the rectal area we can note the fact that in evolution, 1 out of 2 patients with proctitis will develop a left colitis, 1 out of 3 patients will develop an extended colitis and 1 out of 6 patients will develop a pancolitis. Recent studies prove that the extension rate is significantly increased in patients with proctitis as compared with those with left colitis (4). There are some explanations for these conflicting results. Certain authors report differences in the definition of the extension of the disease with respect to the examination methods (colonoscopy versus barium enema), the anatomical delineation of the boundaries for the lesions designating proctitis (15 cm from anal border) versus proctosigmoiditis or distal form versus extended form (5). Moreover, of great importance is also the microscopic border of the inflammatory lesions, for it is well known that they expand outside the macroscopic delineation. The microscopic extension of the lesions is a better indicative for the assessment of the disease extension than any radiologic or endoscopic modification, an aspect revealed by numerous studies which correlated the risk for colorectal cancer with the microscopic extent of the lesions (6). Factors associated with the extension of the lesions reveal a differentiated involvement in the proximal expansion of the inflammatory lesions. In our study a strong association was ascertained in smokers diagnosed with UC, smoking being regarded as a protective factor for the extension of the lesions, while the non-smokers have a risk almost twice as high (RR = 1.81) (7).

A similar role seems to have the appendectomy (RR = 1.41), although the data in the literature are controversial (8). Additionally, an important correlation is represented by the association of symptoms (especially rectal bleeding) and the extension of the lesions. The relative threefold increased risk of extension in patients with important rectal bleeding highlight the significance born by the intensification of the symptoms as expression of the inflammatory lesion extension, an aspect reported by other authors as well (9). Our data reveal the heterogeneous clinical and evolutionary character of the disease, the continuous chronic activity being less frequent (17,54%) as opposed to the observations reported by other authors (10). We must notice the fact that the proximal extension of the proctitis with the involvement of the left colon or of the entire colon (pancolitis) is statistically significantly correlated with the intermittent chronic forms (p=0.00001). Young patients have a more severe evolution of the disease with respect to the gravity of the disease and the frequency of the relapses associated with the extension of the inflammatory lesions. Our data concurs with the studies which show that the beginning of the disease in young patients and the association with extraintestinal manifestations is predictive for the proximal extension of the lesions. This proves that the age is an important predictive factor for the progression of the disease in the colon associated with the development of the inflammatory process in other organs (11). It seems that the administering of aminosalicylates is more effective in the prevention of the relapses with extension of the lesions as compared with patients who did not receive 5-ASA therapy, although there are some studies which state that maintenance therapy does not significantly influence the extension of the inflammatory lesions (12). The benefits of the long-time corticotherapy were less supported, the extension being very close to that of the patients who did not receive corticotherapy (13).

Conclusions:

The proximal progression of the inflammatory lesions towards extended colitis was recorded both in patients with colitis and left colitis, but with significant differences regarding the mean time of evolution towards pancolitis between proctitis and left colitis. The identification of the main factors associated with the extension could allow a layering of the risk and the elaboration of strategies with successive stages of combination between drug therapy and secondary and tertiary profilactic measures.

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