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The course of colonic disease in ulcerative colitis patients with primary sclerosing cholangitis

Primer sklerozan kolanjiti olan ülseratif kolit hastalarında barsak hastalığının seyri

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Background/aims: *Although there are many studies reporting that colonic dysplasia and cancer develop more frequently in ulcerative colitis patients with ulcerative colitis with primary sclerosing cholangitis, there are insufficient data on the course of the colonic disease. In this study, the course of the colonic disease in ulcerative colitis patients with primary sclerosing cholangitis was investigated.* ***Methods:*** *Data obtained from ten patients with total colitis and accompanying primary sclerosing cholangitis (three females, seven males, mean age: 44.5±10.0 years) were compared with data obtained from 64 patients with pancolitis but without primary sclerosing cholangitis (27 females, 37 males; mean age: 42.3±17.1 years).* ***Results:*** *The follow-up period was 6.4±6.2 years in patients without primary sclerosing cholangitis, 12.7±6.2 years in total and 5.1±4.0 years (after development of the condition) in patients with primary sclerosing cholangitis (p<0.01). The number of disease attacks (3.7 attacks/yr vs. 0.5 attacks/yr), duration of the active disease (12.9±8.0 months vs. 0,3±1.0 months), the number of patients in whom corticosteroids were used (47 patients vs. one patient), the number of patients hospitalized (50 patients vs. one patient) and duration of hospitalization (1.2±0.8 months vs. 0,1±03 months) were higher in patients with than without primary sclerosing cholangitis (after development of the condition) (p<0.001). There was no significant difference in data obtained from patients with and without primary sclerosing cholangitis before development of the disease.* ***Conclusions:*** *Colonic disease subsides when primary sclerosing cholangitis develops. The higher frequency of colonic dysplasia and cancer seen in patients with primary sclerosing cholangitis can be explained by the fact that most of them have a longer duration of total colitis and fewer need total colectomy. Even though it does not seem to cause clinical problems, the colonic disease should not be ignored in these patients.*

Key words: Ulcerative colitis, primary sclerosing cholangitis.

Amaç: *Primer sklerozan kolanjiti olan ülseratif kolit hastalarında kolonda displazi ve kanserin daha fazla geliştiğini bildiren birçok veri olmakla birlikte, barsak hastalığının gidişi hakkında yeterli bilgi mevcut değildir. Bu çalışmanın amacı, primer sklerozan kolanjiti olan ülseratif kolit hastalarında barsak hastalığının gidişini araştırmaktır.* ***Yöntem:*** *Primer sklerozan kolanjiti olmayan 64 (27 K, 37 E, 42.3±17.1 yaş) ve primer sklerozan kolanjiti olan 10 (3 K, 7 E, 44.5±10.0 yaş) pankolitli ülseratif kolit hastalarının verileri karşılaştırıldı. İstatistiksel değerlendirmeler Mann Whitney U, Ki-Kare ve Wilcoxon testleri ile yapıldı.* ***Bulgular:*** *Primer sklerozan kolanjit (-) hastaların izlem süreleri 6.4±6.2 yıl, primer sklerozan kolanjit (+) hastalarının toplam (primer sklerozan kolanjit tanısından önce ve sonraki) izlem süresinden (12.7±6.2) daha kısa (p<0.01) idi; ama primer sklerozan kolanjit geliştikten sonrakinden (5.1±4.0) farklı değildi (p>0.05). Primer sklerozan kolanjit gelişmeyen hastalarda, gelişen hastalara göre takip süresi boyunca atak sayısı (3.7 atak/yıl ve 0.5 atak/yıl), aktif hastalık süresi (12.9±8.0 ay ve 0.3±1.0 ay), kortikosteroid kullanma oranı (47 hasta ve 1 hasta), hastaneye yatma oranı (50 hasta ve 1 hasta) ve hastanede yatış süresi (1.2±0.8 ay ve 0.1±0.3 ay) daha fazla idi (p<0.001). Primer sklerozan kolanjit (-) hastaların verileri, primer sklerozan kolanjit (+) hastaların toplam izlem sürelerindeki verileriyle karşılaştırıldığında, farklılıkların azaldığı ya da ortadan kalktığı görüldü.* ***Sonuç:*** *Primer sklerozan kolanjit geliştiğinde barsak hastalığı yatışmaktadır. Çoğu pankolitli olduğundan ve daha az total kolektomi ihtiyacı gösterdiklerinden uzun süre ülseratif kolitli barsakla yaşamaları bu hastalarda displazi ve kanserin daha sık gelişmesini açıklayabilir. Önemli bir klinik soruna yol açmasa da bu hastaların barsak hastalıklarının ihmal edilmemesi gerekir.*

Anahtar kelimeler: Ülseratif kolit, primer sklerozan kolanjit.

INTRODUCTION

Ulcerative colitis (UC) is a chronic diffuse, mucosal, inflammatory colonic disease of unknown pathogenesis. The disease has a benign course when it involves only the distal and left colon, while it has a severe course and causes systemic symptoms when it involves the whole colon. It is well known that there is a risk of development of malignant conditions in patients with ulcerative

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Table 1. Course of bowel disease in patients with PSC and those without PSC

Parameters	*PSC (-)*	*PSC (+)*[1]	*P*
Number of attacks[2]	3.7	0.5	<0.001
Duration of active disease (month)[3]	12.9±8.0	0.3±1.0	<0.001
Number of patients receiving corticosteroid	47	1	<0.001
Number of patients hospitalized	50	1	<0.001
Length of hospital stay (month)[3]	1.2±0.8	0.1±0.3	<0.001
Number of patients undergoing total colectomy	20	0	0.056

[1]after development of PSC
[2]the number of attacks/year
[3]mean ± standard deviation

colitis, especially in the latter group of patients. The most important risk factors in malignant degeneration of the colon are the duration and extent of the disease (1).

Three to 10 % of patients with UC may develop primary sclerosing cholangitis (PSC). This is frequently diagnosed after detection of UC, though it may be present for many years before UC causes symptoms. Patients with UC and accompanying PSC more frequently develop dysplasia and cancer of the colon (2). Although there have been many studies on the development of malignancy in the colon, there are limited data on the course of the bowel disease.

The aim of this study was to determine whether there is a difference in the course of UC with accompanying PSC and the course of UC alone.

MATERIALS AND METHODS

This study included ten patients with pancolitis and accompanying PSC (three females, seven males; mean age: 44.5±10.0 years) and 64 patients with pancolitis alone (27 females, 37 males; mean age: 42.3±17.1 years) presenting to our outpatient clinic of Inflammatory Bowel Diseases (IBD). Data from patients without PSC were compared with those obtained before and after PSC development in patients with the disease. Parameters obtained before onset of PSC symptoms where then compared with those obtained after onset of PSC symptoms.

Criteria for the diagnosis of UC were typical symptoms and physical findings, supported by radiological and endoscopic features and compatible pathological findings. The diagnosis of PSC was based on the accepted diagnostic criteria (3). These criteria are cholangiographic abnormalities typical of PSC, presence of compatible clinical, biochemical and histological findings and absence of diseases causing secondary sclerosing cholangitis. The time of development of PSC (when early diagnosis of PSC is not made) considered as the time of onset of symptoms in patients with PSC symptoms and as the time when cholestatic parameters, especially alkaline phosphatase, are high in asymptomatic patients. As disease location is the main factor directly affecting the parameters and most patients with PSC also have pancolitis, only patients with pancolitis were included in the study. Pancolitis was considered as disease extending from the anal canal and beyond the hepatic flexure. Endoscopic findings were classified according to Rachmilewitz endoscopic index (4); values of four or more were considered as endoscopic active disease and values of less than four as remission of the disease. Presence of active colitis based on clinical and endoscopic findings was defined as active disease, minimal or no intestinal symptoms and favorable results from endoscopy as remission of the disease and active disease despite medical treatment as continuous disease (5).

Data were collected retrospectively by reviewing patients' records from the IBD outpatient clinic, where patients were followed up regularly. Patients with disease of severe activity were hospitalized, those not needing hospitalization were followed up every three weeks to three months according to severity of disease activity and those in remission were followed up every six to 12 months.

Statistical Analysis: Mann Whitney U test was used for the comparison of mean values, Chi-square for comparison of percentages, Wilcoxon test for comparison of median values and Mc Nemar test for comparison of data obtained by asking yes/no questions.

Table 2. Course of bowel disease before and after diagnosis of PSC

Parameters	*Before PSC*	*After PSC*	*p*
Number of attacks[1]	3.0	0.5	<0.01
Duration of active disease (month)[2]	8.7±4.4	0.3±1.0	<0.05
Number of patients receiving corticosteroid	3	1	>0.05
Number of patients hospitalized	5	1	<0.01
Length of hospital stay (month)[2]	1.1±1.4	0.1±0.3	0.06

[1]the number of attacks/year
[2] mean ± standard deviation

RESULTS

The mean follow-up period of patients without PSC was 6.4±6.2 years and it was shorter than that of patients with PSC (12.7±6.2) (p<0.01), but not different from the follow-up period after diagnosis of PSC (5.1±4.0 years) (p>0.05).

The number of attacks, number of patients who had used corticosteroids, number of patients hospitalized, length of hospital stay and need for total colectomy were low in patients with PSC compared to those without PSC (Table 1). Colitis was not continuous after the onset of UC in any patient with both UC and accompanying PSC, while it was continuous in 17 patients without PSC (26.6%), with no significant difference (p=0.104).

There was a significant difference between data obtained before development of symptoms and those obtained after development of symptoms in patients with PSC, although the significance was low.(Table 2).

There was no significant difference in data obtained from patients without PSC and data obtained from patients with PSC prior to the development of PSC symptoms (Table 3).

DISCUSSION

The results of this study show that morbidity due to colonic disease activity was considerably less in patients with UC and accompanying PSC than those with UC alone.

It may seem that the rate of PSC reported in this study (ten of 74 patients with UC had PSC) is high compared to that reported in the literature. However, when all of the patients with UC attending our clinic are considered, the frequency of UC accompanied by PSC is similar to the established rate (2.3%) (6). The difference can be explained by the fact that PSC occurs more frequently in patients with pancolitis. Since the patients included in this study had pancolitis, the rate of continuous colitis was high (26.6%). The rate of total colectomy (31.2%) was not surprising for the mean follow-up period of 6.4±6.2 years (1-26 years).

Table 3. Course of bowel disease before development of PSC in patients with PSC and those without PSC

Parameters	*PSC (-)*	*PSC (+)π*	*p*
Number of attacks[2]	3.7	3.0	>0.05
Duration of active disease (month)[3]	12.9±8.0	8.7±4.4	>0.05
Number of patients receiving corticosteroid	47	3	>0.05
Number of patients hospitalized	50	5	>0.05
Length of hospital stay (month)[3]	1.2±0.8	1.3±1.4	>0.05
Number of patients undergoing total colectomy	20	0	>0.05

[1]before development of PSC
[2]the number of attacks/year
[3]mean ± standard deviation

The most important factor determining the course and prognosis of UC are extent and duration of disease. To date, studies have generally employed the need for total colectomy and dyplasia and/or development of malignancy as the prognostic parameter. Thus the risk of malignancy and need for total colectomy increases in patients with protracted pancolitis. The cumulative risk for colorectal cancer in patients with UC was estimated to be 1.8% at 20 years and 43% at 35 years (7,8). The possibility of colorectal cancer was found to be 1.7% in patients with proctocolitis, 2.8% in those with limited disease (not beyond the hepatic flexure) and 14.8% in those with extensive disease (9).

Ulcerative colitis accompanied by of PSC increases the possibility of malignancy. Follow-up using colonoscopic examinations showed that 46% of patients with UC associated with PSC and 16% of those with UC only were found to have dysplasia (10). In another study, the possibility of intestinal dysplasia or cancer was reported to be 50% in patients with a 25 year history of UC and PSC and 10% in patients with UC only (11).

The reason why colonic cancer develops more frequently in patients with UC and accompanying PSC is not clear. These patients were shown to have anaploidy six times as high as those with UC alone (10); anaploidy is known to predispose to development of colonic cancer and play an important role in the development of dysplasia into cancer (1).

Based on the fact that a protracted course of UC is directly related to colonic cancer, it may be claimed that bowel disease has a low activity in patients with PSC; thus colectomy is required less frequently. The presence of more protracted bowel disease also increases the risk of colonic cancer.

In this study, however patients with bowel disease were followed up for a long time without any problem. Similarly, one study, found that systemic or local corticosteroids were less frequently used in patients with PSC and that the rate of hospitalization in these patients was lower (12). In another study, however, the majority of patients with PSC but without symptoms of bowel disease were reported to have inflammatory bowel disease based on colonic examination. It was also emphasized that late detection of inflammatory bowel disease could lead to colonic cancer (13). Patients with high disease activity undergo total colectomy and this operation removes the risk of colonic cancer, but the same cannot be said for patients with UC and accompanying PSC (1).

Further studies may elucidate whether the lower activity of UC in the presence of PSC is the result of a change in pathogenesis of UC and whether this change increases the risk of colonic cancer. Our finding that the clinical course of bowel disease was similar to that of patients with PSC before the onset of PSC symptoms (Table 3), suggests the influence of PSC on the severity of bowel disease.

It may be concluded that bowel diseases in patients with UC and accompanying PSC should not be regarded complacently and that they should be followed up regularly in view of the high risk of colonic cancer, even when the bowel disease settles down.

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