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The frequency of sacroileitis and ankylosing spondylitis in inflammatory bowel disease and HLA-B27 association

İnflamatuar bağırsak hastalıklarında sakroileitis, ankilozan spondilitis sıklığı ve HLA-B27 birlikteliği

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Background/aims : *The aim of this study was to investigate the frequency of sacroileitis and ankylosing spondylitis in inflammatory bowel disease and the relationship between disease activity, joint symptoms and HLA-B27 antigen positivity.* ***Methods:*** *Sacroiliac joint radiography and three phase bone scanning of 33 ulcerative colitis patients (17 active and 16 in remission) and 29 Crohn's disease patients (15 active and 14 in remission) was performed. HLA-B27 was determined in all patients and 60 control subjects.* ***Results:*** *Sacroileitis was found in 10 out of 33 patients with ulcerative colitis (30. 30%) and seven out of 29 patients with Crohn's disease (24. 13%). Of these patients, eleven had active (17.73%) disease and six were in remission (9. 68%). The diagnosis of sacroileitis was made by bone radiography in seven patients (41.18%) and by bone scanning in the other 10 patients (58.82%). A diagnosis of ankylosing spondylitis was made in three patients (17. 64%) who had previously been diagnosed by bone radiography to have sacroileitis. HLA-B27 was positive in six patients (9.67%) with inflammatory bowel disease and three subjects (5%) of the control group. There were no significant differences between these two groups (p>0.05). Compared to the control group, all three patients with ankylosing spondylitis were HLA-B27 positive, the difference being significant (p>0. 01).* ***Conclusions:*** *The clinical course of sacroileitis is independent of the activitiy of inflammatory bowel disease. Accordingly, patients with inflammatory bowel disease, especially those with sacroileitis, should be investigated for the presence of anklylosing spondylitis. .*

Key words: Ankylosing spondylitis, Crohn's disease, sacroileitis, ulcerative colitis, HLA-B27.

Amaç: *İnflamatuar bağırsak hastalıklarında ankilozan spondilitis ve sacroileitis sıklığı, eklem semptomları ile hastalık aktivasyonu ilişkileri ve HLA-B27 antijen pozitifliğini araştırdık.* ***Yöntem:*** *33 ülseratif kolitli hastada (17 aktif ve 16 remusyon) ve 29 crohnlu hastada (15 aktif ve 14 remusyon) sakroiliak eklemden üç fazlı kemik sintigrafisi ile direkt kemik grafisi çektirdik. Tüm hastalarda ve 60 kontrol grubunda HLA-B27 antijen çalıştık.* ***Bulgular:*** *Ülseratif kolitli 33 hastanın 10'da (%30.3) ve crohnlu 29 hastanın 7'de (%24.13) sakroileitis saptadık. Bu hastaların 11'i aktif (%17. 73), 6'sı remusyon (%9.68) grubunda idi. Sakroileitis teşhisini 7 hastada kemik grafisi (%41.18), 10 hastada kemik sintigrafisi (%58. 82) ile tespit ettik. Kemik grafisi ile sakroileitis tespit ettiğimiz hastaların 3'ü (%17.64) ankilozan spondilitis tanısı aldı. HLA-B27 pozitifliği inflamatuar barğırsak hastalıklarında 6 (%9. 67), kontrol grubunda 3(%5) idi. Bu iki grup arasında anlamalı fark yoktu (P>0. 05). Ankilozan spondilitisli 3 hastada HLA-B27 pozitifdi ve bu kontrol grubuna göre anlamlı idi (P<0. 01).* ***Sonuç:*** *Sakroileitisin klinik seyri bağırsaktaki inflamatuar aktiviteden bağımsızdır. İnflamatuar bağırsak hastalıkları ve özellikle sakroileitis saptanmış olanlar ankilozan spondilits yönünden araştırılmalıdır.*

Anahtar kelimeler: Ankilozan spondilitis, Crohn hastalığı, sacroileitis, ülseratif kolitis, HLA-B27.

INTRODUCTION

Ulcerative colitis (UC) and Crohn's disease (CD) are chronic and idiopathic inflammatory diseases of the gastrointestinal tract. Despite significant differences between both entities, they are generally accepted under the term of inflammatory bowel disease (IBD) (1,2). There may be both systemic and local complications of IBD, with one of the most important extraintestinal manifestations being joint complications (3,4).

Lower back pain and limitation in joint movements can be encountered in patients with symptomatic sacroilitis (5-7). In IBD, asymptomatic involvement can be shown by radioisotopic bone scanning methods. Furthermore, different activities of arthritis can be shown by a series of bone scans (8,9). The early radiographic feature of sacroileitis is erosion; in the latter stage, in addition to erosion, there is narrowing of the joint

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Table 1. General features of IBD patients and controls

	Ulcerative Colitis (UC)		*Crohn's Disease* (UC)		*Controls*
	Active (n)	*Remission (n)*	*Active (n)*	*Remission (n)*	
Patients (N)	17	16	15	14	60
Male	9	5	8	7	33
Female	8	11	7	7	27
Age	43.87± 11.97	42.56±10.45	41.24±12.83	14.31±12.83	31.12±12.47
EAI	7.82±2.32	1.75±1.29			
CD activity index	7.64±1.51	1.28±1.19			
Sacroiliitis	5	5	6	1	-
Ankylosing spondiylitis	-	1	1	1	-

space with sclerosing, ankylosing and even complete fusion. The degree of erosion is then more easily demonstrable by computed tomography (CT) and magnetic resonance imaging (MR) (9,10).

The type of sacroileitis seen in IBD is of the seronegative arthritis group. It is thought that in ankylosing spondylitis, the passage of gram negative microorganisms via the intestinal wall leads to stimulation of antigen factor formation in HLA-B27 (11,12).

Spondyloarthropathies can progress to ankylosing spondylitis. Many subclinical IBD diagnoses are made during ileocolonoscopic examination of cases with ankylosing spondylitis (11,13).

MATERIALS AND METHODS

In this study, a total of 62 IBD patients (33 UC, 29 CD) and 60 healthy control subjects were included. Patients with rheumatoid arthritis (RA), Reiter's syndrome disorders of connective tissue and psoriasis were excluded. Diagnosis of UC and CD was made by clinical, endoscopic and histological findings. The disease activitiy in UC was evaluated with Rachmilewitzs endoscopic activitiy index (EAI). An EAI>4 was accepted to represent active UC (1). Assessment of disease activity in CD was made using the simple index (14). If the disease activity index was more than or equal to six points, it was accepted to represent active CD. The control group had various gastrointestinal complaints but no proven disease of the small or large bowel according to laboratory and endoscopic findings. Conventional radiographies of the sacroiliac joint in an appropriate position were performed in all cases of UC and CD study group patients by evaluation of right and left sacroiliac joint films. The presence and degree of sacroillitis was determined.

Three phase bone scanning was also performed in all cases of UC and CD, prior to which intravenous injection of TC-99m MDP (methyl diphosfonate) was administered. After the procedure, early dynamic static images and late static images three hours later were obtained from the sacroiliac joint. In all cases, the right and left sacroiliac index (SIE) was measured. Patients with SIE above 1. 30 were diagnosed with sacroileitis and evaluated for ankylosing spondylitis according to modified New York criteria. The blood sample for HLA-B27 evaluation in all 62 patients with IBD and 60 control groups cases was analysed in apparatus of FACS flow cytometer. (Becton Diclinson). Levels of HLA-B27 were determined as previously described (20,21). Comparison of quantitative parameters between patients with UC, CD and controls was undertaken using Kruskal Wallis or Mann-Whitney U tests. For comparison of qualitative parameters, chi-square analysis was used, with $p<0.0.5$ being accepted as significant.

RESULTS

The demographic features of 33 UC, 29 CD and 62 control cases and activitiy indexes of UC and CD patients are summarized in Table I. Of 62 cases of IBD, 17 (27.41%) had sacroileitis. Ten cases (30.30%) of 33 patients with UC and seven (24.13%) of 29 patients with CD had sacroileitis. Further evaluation of the 62 IBD cases revealed that 17 had sacroileitis. Of these, 11 (17.73%) had

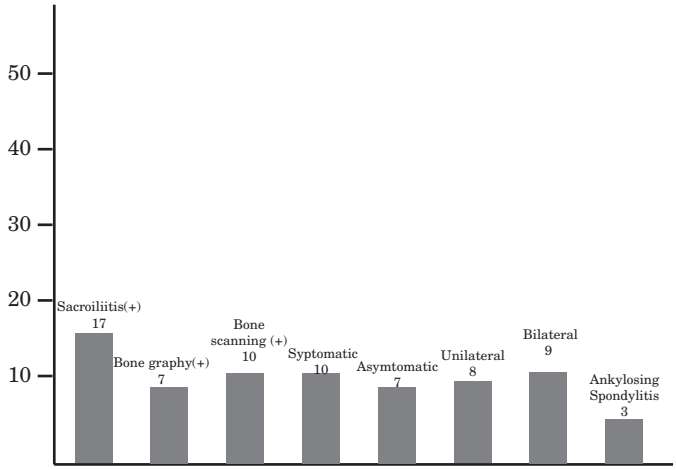

Figure 1. The assessment of sacroiliitis patients.

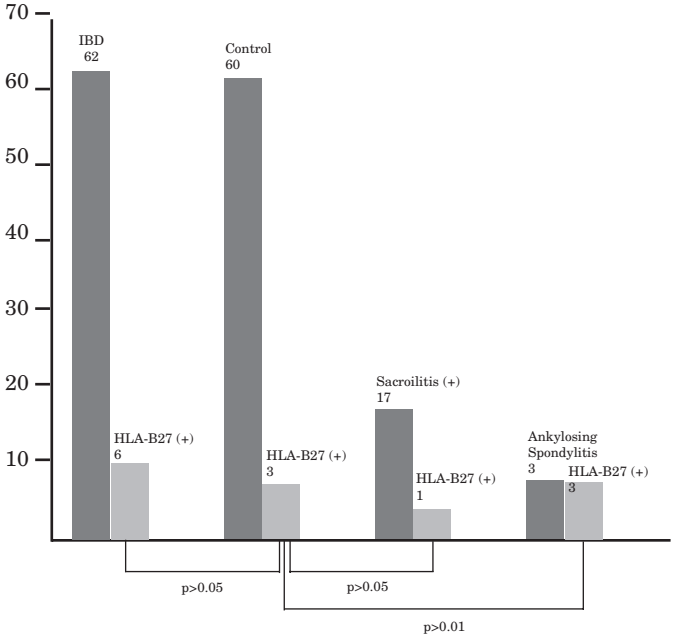

Figure 2. General properties of HLA-B27 positive patients.

active disease and the other six (9.69%) were in remission. There was no significant difference between active and remission cases (p>0.05) (Table 2). Ten patients (58.82%) with sacroileitis were identified by bone scintigraphy while the other seven (41.8%) were identifield by bone radiography. Patients who were identified by bone radiography to have sacroileitis were later diagnosed to have ankylosing spondylitis. Thus there were three (4.83%) ankylosing spondylitis cases among 62 IBD patients. Of these three patients, two had CD and one had UC. On the other hand, no patients identified by bone scanning to have sacroileitis had ankylosing spondylitis. Of the 10 patients with sacroileitis identified by bone scanning, three had joint symptoms (17.64%) and seven had no joint symptoms (41.17%). Five patients had bilateral sacroileitis while the other five had unilateral disease.

All patients with sacroileitis diagnosed by bone radiograhpy had joint symptoms; four patients in this group had bilateral and three had unilateral disease (Figure 1).

HLA-B27 positivity was 9.67% among IBD patients (six cases) and 5% among control subjects (three cases). There was no significant difference in HLA-B27 positivity (p>0.05) between the IBD patients and control subjects. All three ankylosing spondylitis cases were HLA-B27 positive (100%) making the statistical difference significant when compared to HLA- positivity among control subjects (p<0. 01) (Figure2).

Table 2. The distribution of sacroiliitis in IBD cases :

	Ulcerative colit (UC) *n:33*	*Crohn's diseases (CD)* n:29
Sacroiliitis (+) n:17 (27.41%)	n:10 (30. 30%) *Active n:5 (15.15%) *Remission n:5 15.15%)	n:7 (24. 13%) *Active n:6 (20.68%) *Remission n:1 (3.45%)
n:62	Sacroiliitis (+) active IBH. n: 11 (17.73%) Sacroiliitis (+) remission IBH. n: 6 (9.68%)	

The statistical significance of sacroiliitis cases

Px = UC - CD	p>0.05
Pxx = UC (active) – UC (remission)	p>0.05
Pxxx = CD (active) – CD (remission)	p>0.05
Pxxxx =IBD (active) – IBD (remission)	p>0.05

DISCUSSION

In IBD, sacroileitis is the most important extraintestinal manifestation (1,4). IBD is frequently associated with the clinical features of spondylitis which are similar to these of idiopathic ankylosing spondylitis. The inital symptoms are insidious lower back pain and morning stiffness. These symptoms decrease with exercise and are aggravated by bed rest. Deker-Saeys et al. have shown that in IBD, the incidence of sacroileitis is about 10% (16), while Mielants et al. found it to be about 5-12% (6). Gravallese et al. have shown that asymptomic sacroileitis can be diagnosed with bone scanning and that its incidence in IBD is about 52% (7).

In this study we found the incidence of sacroileitis in IBD, UC and CD cases to be 27.41%, 30.30% and 24.3% respectively. Some findings of sacroileitis like hyperemia and inflammation of joints can not be demonstrated by bone radiography. Bone scanning is essential for evaluation of sacroileitis among IBD cases and for investigation of asymptomatic patients. Furthermore, it is also essential in the diagnosis and follow-up of cases with bilateral sacroileitis. Determination of the sacroileitis index facilitates more objective decision making and many previous studies have shown the incidence of sacroileitis among IBD, UC and CD patients to be similar (7,12,16).

In this study, although the incidence of sacroileitis in UC cases was more frequent in comparison to CD, there was no significant difference ($p>0.05$). In contrast to peripheral arthritis, the clinical progress of sacroileitis and spondylitis in IBD is independent of inflammatory activity in the bowel (1-3,5). In some cases, the diagnosis of IBD is reached after a diagnosis of sacroileitis and spondyloarthropathy. Treatment of IBD has no effect on the clinical progress and incidence of sacroileitis.

In contrast to spondylitis associated with IBD, there is no increase in the incidence of HLA-B27 in most patients with sacroileitis. The sacroileitis affecting the spinal vertebra in IBD is symmetrical and may progress to complete ankylosis of the sacroliac joint, thus HLA-B27 positive cases of IBD may be at risk of developing spondylitis. In various reports, it is shown that the incidence of ankylosing spondylitis in IBD is about 4% (6,16,17), but in our study the incidence was approximately 4.83%. As sacroileitis occurs in the early stage of ankylosing spondylitis, IBD cases should be evaluated for this disease It is also necessary to investigate IBD as a possible etiologic factor of ankylosing spondylitis as there are patients with ankylosing spondylitis in whom subclinical IBD has been diagnosed by ileocolonoscopy.

Many studies have shown that central arthritis is more prevalent than peripheral arthritis in IBD, increasing with posivitiy of HLA-B27 (1,2,4,18,19). In a variety of reports, it has been shown that in sacroileitis, the incidence of HLA-B27 positivity is about 20-53% (7,18). In our study the incidence of HLA-B27 positivity in IBD was about 9.67%. Many studies have shown that in IBD associated with ankylosing spondylitis, the incidence of HLA-B27 positivity is about 80% (7,18,19). It is therefore concluded that HLA-B27 positive sacroilitis patients should be followed up closely for the development of ankylosing spondylitis.

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