ARTHRITIS ASSOCIATED WITH ULCERATIVE COLITIS*

BY

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Previous reports indicate that arthritis occurs in association with ulcerative colitis in excess of the incidence which would be expected in the general population. Approximately 2·5 per cent. of the general population have a form of arthritis according to Woolsey (1952) and Cobb and Lawrence (1957). Depending on the criteria used for diagnosis, arthritis occurs in 7 to 20 per cent. of patients with ulcerative colitis (Hench and 5 others, 1936; Bargaen, Jackman, and Kerr, 1938; Jankelsen, McClure, and Sweetsir, 1942; Ricketts and Palmer, 1946; Hench and 10 others, 1948; Kirsner, Palmer, Maimon, and Ricketts, 1948; Sloan, Bargaen, and Gage, 1950; Brown, Kasich, and Weingarten, 1951).

Until 1959 it was believed that the most common type of arthritis found in patients with ulcerative colitis was rheumatoid arthritis (Bywaters and Ansell, 1958; Ford and Vallis, 1959; Friedman and Kehoe, 1959; McEwen, Ziff, Carmel, DiTata, and Tanner, 1958). Since then several well-documented reports have indicated that ankylosing spondylitis is found more commonly than is expected in the general population and may be the most frequent type of inflammatory arthritis which develops in patients with ulcerative colitis (Acheson, 1960; Fernandez-Herlihy, 1959; Zvaifler and Martel, 1960). One of the authors (J.R.) has seen nine patients with ulcerative colitis and arthritis. In addition Montefiore Hospital has a tradition of careful follow-up of patients with chronic disease. Therefore these several reports prompted an evaluation of our hospital population with ulcerative colitis in order to determine the incidence and forms of arthritis which occur in them.

Material

All patients with an established diagnosis of ulcerative colitis seen at Montefiore Hospital from 1939 to 1961 are included in this study, a total of 333 (173 females and 160 males). Of the 333 patients with ulcerative colitis, 78 had a tissue diagnosis made by biopsy, laparotomy, or autopsy. In addition, 211 patients had one or more barium enemas, which were diagnostic of ulcerative colitis, or contributed (with proctoscopy and/or tissue biopsy) to the establishment of the diagnosis of ulcerative colitis. In 111 patients proctoscopic examinations were made which aided in the diagnosis of bowel disease; significantly, in 107 of these patients at least one other procedure was performed in order to establish the diagnosis of ulcerative colitis. In 38 of the earliest cases in this study a G.I. series was carried out, without barium enema, but with proctoscopy, in order to establish the diagnosis of ulcerative colitis.

In reviewing the 333 established cases of ulcerative colitis, the authors were impressed by the multiplicity and repetition of procedures in most of the patients even after the diagnosis was firmly established.

Results

It was found that 34 patients with ulcerative colitis (10·2 per cent.) had arthritis. Eleven (3·3 per cent.) had degenerative joint disease (osteoarthritis) diagnosed by clinical data and x-ray studies.

The other 23 had inflammatory arthritis (Table, opposite).

Nine of these (2·7 per cent.) had ankylosing spondylitis diagnosed by radiological evidence of sacro-iliac and/or vertebral joint involvement and paravertebral ligament calcification and absence of the rheumatoid factor in the serum (Boland and Present, 1945; Wilkinson and Bywaters, 1958).

Six patients (1·8 per cent.) had definite rheumatoid arthritis diagnosed by the criteria of the American Rheumatism Association (Ropes, Bennett, Cobb, Jacox, and Jessar, 1957, 1959) and a positive test for the rheumatoid factor.

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TABLE

TEMPORAL RELATIONSHIP OF OCCURRENCE OF ULCERATIVE COLITIS AND ARTHRITIS, BY TYPE OF INFLAMMATORY ARTHRITIS

Sex	Diagnosis	Age (yrs)			First Symptoms
		At Onset of Ulcerative Colitis	At Onset of Arthritis	Interval	
M	Ankylosing Spondylitis	49	9	40	A
M		15	13	2	A
M		53	50	3	A
M		20	20	0	Same
M		18	21	3	C
M		44	42	2	A
M		41	38	3	A
F		40	46	6	C
F		38	24	14	A
F	Definite Rheumatoid Arthritis	35	7	28	A
F		22	29	7	C
F		69	64	5	A
F		38	44	6	C
M		16	24	8	C
F		34	38	4	C
M	Psoriatic Arthropathy	37	39	2	C
M		33	20	13	A
F		42	40	2	A
M	Undefined Arthritis	36	38	2	C
F		51	55	4	C
M		38	33	5	A
M	Gout	61	35	26	A
M		51	51	0	Same

Three patients (0.9 per cent.) had psoriatic arthropathy diagnosed by dermatological signs with typical peripheral joint involvement and an absence of rheumatoid factor.

Three patients (0.9 per cent.) had undefined arthritis, showing symptoms and signs of arthritis but not meeting the criteria of the American Rheumatism Association for any defined category. No characteristic pattern of arthritis could be discerned in this group.

Two patients (0.6 per cent.) had gout diagnosed by hyperuricaemia, radiological changes and tophaceous deposits of uric acid.

There was a slight tendency for the arthritis to occur before the bowel disease (52 : 48 per cent.). In the patients with ankylosing spondylitis the male : female ratio was 7 : 2. A review of each case with ulcerative colitis and arthritis revealed no relationship between exacerbations of the bowel disease and the arthritic state. An exacerbation of activity in one disease was as likely to occur independently without reactivation of the other as not.

Discussion

In his study of 555 patients with ulcerative colitis, Fernandez-Herlihy (1959) found that the disease occurred in a sex ratio of 52.3 per cent. females to 47.7 per cent. males, and that in approximately

25 per cent. of these patients the onset of the disease occurred between 20 and 29 years of age. Our study revealed exactly the same sex ratio and age at onsets Brown and others (1951) reported an incidence of 7.5 per cent. of arthritis in their study of 147 cases of ulcerative colitis. Kirsner and others (1948) found that 8 per cent. of patients with ulcerative colitis had arthritis. Coinciding with these findings, 10.2 per cent. of our patients had arthritis. The incidence of arthritis in the general population is between 1.5 and 2.5 per cent.; therefore, the incidence of arthritis in patients with ulcerative colitis is at least four times the expected figure in the general population.

Bywaters and Ansell (1958) published a significant report of 109 cases of ulcerative colitis, 37 of which had arthritis. On the basis of their observations they concluded that a "separate form" of arthritis was most commonly associated with ulcerative colitis. Essentially, this was an asymmetrical arthritis more commonly affecting the lower than the upper extremities with a subacute synovitis and a negative differential agglutination test for rheumatoid factor. Significantly, they noted that six patients had marked sacro-iliac joint changes indistinguishable from those of ankylosing spondylitis, and in these cases, as in other cases in this study, the peripheral arthritis affected those joints commonly afflicted in ankylosing spondylitis. Despite these similarities to ankylosing spondylitis the authors preferred to classify this form of arthritis as a type of arthritis specific to patients with ulcerative colitis.

Since the report by Bywaters and Ansell, several groups of workers have analysed their cases of arthritis associated with ulcerative colitis, and Zvaifler and Martel (1960), Acheson (1960), McEwen and others (1958), McEwen (1960), and McEwen, Lingg, Kirsner, and Spencer (1962) have published carefully analysed studies. They have concluded that there is significant evidence to indicate that ankylosing spondylitis occurs with unexpectedly great frequency in patients with ulcerative colitis. Zvaifler and Martel (1960) studied 100 consecutive unselected patients with ulcerative colitis, and found that 6 per cent. had ankylosing spondylitis. Acheson (1960) carried out a retrospective study of the case records of 2,000 patients with ulcerative colitis and regional ileitis, and found a 20-fold increase in the frequency of ankylosing spondylitis in these patients over the expected figure in the general population. Neither of these studies reported an increased incidence of rheumatoid arthritis or the occurrence of an arthritis specific to patients with ulcerative colitis. McEwen and his associates (1958, 1960, 1962) have reported a study of 32 cases of ulcerative

colitis with arthritis and have recently added an additional forty cases to the original group. In the original report and the total of 72 cases, 25 per cent. had ankylosing spondylitis. This, as in Acheson's study, reflects a 20-fold increase in the expected frequency of ankylosing spondylitis in these patients. In addition to the large number of spondylitics, McEwen and his associates found a specific type of arthritis, like that described by Bywaters and Ansell, occurring with great frequency in their patients. This specific type of arthritis was the most frequent inflammatory arthritis in this group of patients.

In our study of 333 patients with ulcerative colitis, there was a 2.7 per cent. occurrence of ankylosing spondylitis and a 1.5 per cent. occurrence of rheumatoid arthritis, a case occurrence ratio of 1.7 : 1. In the general population the occurrence of ankylosing spondylitis is .05 per cent. and that of rheumatoid arthritis is 1.2 per cent., a case occurrence of 1 : 24 (Woolsey, 1952; Cobb and Lawrence, 1957). These results indicate that our patients have a 50-fold increase of ankylosing spondylitis over the expected figure, a normal incidence of rheumatoid arthritis, and a 40-fold reversal of the case occurrence ratio. We did not encounter among our patients with ulcerative colitis and arthritis a specific type of arthritis different from ankylosing spondylitis and rheumatoid arthritis.

The normal sex ratio of men to women in patients with ankylosing spondylitis is 13 : 1 (Zvaifler and Martel, 1960). The patients reported by these authors had a sex ratio of 3 : 1. The patients with ankylosing spondylitis reported by McEwen (1960) had a sex ratio of 13 : 1. Our study indicates that patients with ulcerative colitis and ankylosing spondylitis have a sex ratio of 7 : 2; this figure is in accord with Zvaifler and Martel's data, and may indicate a slightly higher occurrence of female spondylitics in patients with ulcerative colitis than in the spondylitics in the general population. The sex ratio of rheumatoid arthritis in patients with ulcerative colitis (five females to one male) is the same as the figure expected in the general population.

In each of the three reports in which ankylosing spondylitis was frequently associated with ulcerative colitis, there was a marked tendency for the arthritis to precede the onset of the bowel disease, frequently by many years (Acheson, 1960; McEwen, 1960; Zvaifler and Martel, 1960). Our study is not as striking in this aspect as the previous reports. Six of nine patients developed ankylosing spondylitis before ulcerative colitis. McEwen (1960) stated that "it is generally agreed in all reports that

arthritis and colitis tend to flare together". However, in his studies, such parallelism was lacking in at least one-third of the patients. We could find no evidence of the existence of such a parallelism in a majority of our patients. There were as many simultaneous exacerbations of the two disease processes as there were individual exacerbations.

In the important aspects of this report our data concur with, and extend, the data of Acheson (1960), McEwen (1960), Zvaifler and Martel (1960), and McEwen and others (1962) indicating that there is a marked increase in the frequency of the occurrence of ankylosing spondylitis in patients with ulcerative colitis. Ankylosing spondylitis was the most commonly occurring inflammatory arthritis in patients with ulcerative colitis. We did not find the specific type of arthritis which has been described by these authors and by Bywaters and Ansell (1958). However, this "specific" type of arthritis has many similarities to ankylosing spondylitis, and a future follow-up may reveal that these patients also had ankylosing spondylitis. Since there are now several groups of carefully analysed patients, it should become clear in the future whether or not a type of arthritis specific to patients with ulcerative colitis exists or whether it is, in fact, ankylosing spondylitis. We, like other workers in the field, can give no explanation for the increased frequency of ankylosing spondylitis in patients with ulcerative colitis.

Summary

(1) Of 333 unselected consecutive cases of ulcerative colitis seen at Montefiore Hospital in the past 22 years, 2.7 per cent. had ankylosing spondylitis and 1.5 per cent. had rheumatoid arthritis.

(2) These findings represent a 50-fold increase in the frequency of the occurrence of ankylosing spondylitis in patients with ulcerative colitis over the expected incidence in the general population, and a normal incidence of rheumatoid arthritis.

(3) We found no data to support the idea of an arthritis specific to patients with ulcerative colitis and different from ankylosing spondylitis and rheumatoid arthritis.

(4) Our data indicate that there is a higher proportion of female cases of spondylitis among the patients with ankylosing spondylitis and ulcerative colitis. Ankylosing spondylitis occurred before ulcerative colitis in a small majority of cases. We found no evidence of the synchronous exacerbation of arthritis and colitis in the same patient.

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Arthrite associée à la colite ulcération

RÉSUMÉ

(1) Parmi 333 cas consécutifs, sans sélection, de colite ulcération vus à l'hôpital Montefiore pendant les derniers 22 ans, il y eut 2,7% des cas de spondylarthrite ankylosante et 1,5% d'arthrite rhumatismale.

(2) Cela représente une fréquence de la spondylarthrite ankylosante cinquante fois plus grande parmi les malades atteints de colite ulcération que dans la population générale et une fréquence normale de l'arthrite rhumatismale.

(3) Nous n'avons pas trouvé de preuves d'existence d'une arthrite spécifique des malades atteints de colite ulcération et différente de celle rencontrée dans la spondylarthrite ankylosante ou l'arthrite rhumatismale.

(4) Nos chiffres indiquent que la proportion des cas féminins de spondylarthrite est augmentée chez les malades atteints de spondylarthrite ankylosante et de colite ulcération. Dans une petite majorité des cas la spondylarthrite ankylosante survenait avant la colite ulcération. Nous n'avons pas trouvé d'exacerbations simultanées de colite et d'arthrite chez le même malade.

Artritis asociada a la colitis ulcerativa

SUMARIO

(1) Entre 333 casos consecutivos, sin selección, de colitis ulcerativa, vistos en el hospital Montefiore durante los últimos 22 años, hubo un 2,7% casos de espondil-artritis anquilosante y un 1,5% casos de artritis reumatoide.

(2) Esto representa una frecuencia de espondil-artritis anquilosante cincuenta veces más grande en los enfermos con colitis ulcerativa que en la población general y una frecuencia normal de la artritis reumatoide.

(3) No se encontraron pruebas de existencia de una artritis específica de enfermos con colitis ulcerativa y diferente de la observada en enfermos con espondil-artritis anquilosante o con artritis reumatoide.

(4) Nuestros datos indican una mayor proporción de casos femeninos de espondil-artritis en enfermos con espondil-artritis y colitis ulcerativa. En una pequeña mayoría de los casos la espondil-artritis anquilosante se presentaba antes de la colitis ulcerativa. No se observaron exacerbaciones simultáneas de colitis y de artritis en el mismo enfermo.