Fibromyalgia in patients with rheumatoid arthritis is associated with higher scores of disability

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Rheumatoid arthritis (RA) is a chronic polyarticular disease characterised by pain in peripheral joints accompanied by swelling, stiffness, and functional impairment. In some cases it is associated with fibromyalgia (FM), a syndrome defined by chronic, widespread pain, asthenia, and sleep disorders. When a patient has both RA and FM, determining the degree of RA activity may be difficult, because these patients typically have higher scores for pain and disability.

This study aimed at evaluating whether there were differences in functional disability, extra-articular manifestations, and use of disease modifying antirheumatic drugs (DMARDs), between patients with RA with and without FM.

PATIENTS AND METHODS

A cross sectional study was conducted with 386 patients with RA, 94 men and 292 women, with a mean age of 53 years. All the patients met the criteria of the American College of Rheumatology (ACR) for the diagnosis of the disease.[1] The mean duration of the disease was nine years. All the patients received treatment in a hospital outpatient clinic and were included in a database between 1991 and 2000. To diagnose FM, ACR criteria had to be fulfilled on at least two consecutive visits.[2] The following assessment was made in all patients participating in the study: a clinical history, evaluation of functional status using the Health Assessment Questionnaire (HAQ),[3] conventional laboratory measurements, and evaluation of the rheumatoid factor. In addition to these assessments, extra-articular manifestations were diagnosed. Secondary Sjögren's syndrome was diagnosed when, in addition to subjective xerophthalmia and xerostomia, Schirmer's test or the rose bengal staining were pathological.[4] The number of previous DMARDs was counted, independently of whether the patient received a single drug or a combination.

Contingency tables were used to compare the frequency of categorical variables among the different groups. To compare numerical variables we used Student's *t* test when the data followed a normal distribution and the equivalent Wilcoxon non-parametric test when they did not.

RESULTS

Of the total, 57 (14.8%) patients fulfilled FM criteria. No differences were found in age or disease duration between patients with RA without FM (RA group) and patients with RA and FM (RA-FM group) (table 1). In the RA-FM group there was a higher percentage of women (p=0.03); HAQ scores (p=0.002) were also higher. The incidence of extra-articular manifestations such as serositis, pneumonitis, or Sjögren's syndrome was similar in both groups. Rheumatoid nodules and the rheumatoid factor were more common in the RA group, although differences were not significant. The RA-FM group had received a greater number of DMARDs (p=0.04).

DISCUSSION

The results of this study indicate that patients with RA who also have FM are more often women, have higher disability scores, and receive DMARDs more frequently.

Wolfe *et al* studied 242 patients with RA and 38 who had FM occurring in association with RA. The RA-FM group had more abnormal measures of function, pain, disease activity, and psychological status, but the disease severity in RA-FM and RA was similar.[5] In patients with RA, FM tender points have been found to correlate mainly with daily stress and with higher joint tenderness count scores, indicating that patients with RA and FM have a lower pain threshold.[6 7] Patients with RA and depression often perform fewer daily life activities.[8]

In summary, FM is found to be associated in one of seven patients with RA; the presence of FM may constitute a marker of a worse prognosis for subjective functional disability.

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Table 1 Comparison of patients with rheumatoid arthritis (RA) and rheumatoid arthritis and fibromyalgia (RA-FM)

	RA-FM	RA	p Value
Number of patients	57	329	
Women (No (%))	50 (88)	242 (74)	0.03
Mean (SD) age (years)	52 (9.6)	53 (15)	0.42
Duration of RA disease (SD), years	8 (8)	9 (9)	0.35
HAQ (mean (SD))	1.62 (0.70)	1.21 (0.77)	0.002
Patients with rheumatoid factor (No (%))	37 (65)	247 (75)	0.13
Extra-articular manifestations			
Rheumatoid nodules (No (%))	10 (18)	82 (25)	0.36
Secondary Sjögren's syndrome (No (%))	15 (26)	80 (24)	0.97
Serositis (No (%))	3 (5)	12 (4)	0.99
Interstitial lung disease (No (%))	0	17 (5)	
Number of DMARDs (mean (SD))	2.64 (1.6)	2.17 (1.5)	0.04

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Shingles following infliximab infusion

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Infliximab is a chimeric IgG1κ monoclonal antibody that binds specifically to human tumour necrosis factor alpha (TNFα). Infliximab, in combination with methotrexate, is approved for reducing signs and symptoms and inhibiting the progression of structural damage in patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to methotrexate. It will also reduce the signs and symptoms of Crohn's disease in patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional treatment and will reduce the number of draining enterocutaneous fistulas in patients with fistulising Crohn's disease.[1 2] Owing to its mechanism of action infliximab can lead to a number of complications.

CASE REPORT

Here we report a case of shingles, an infectious complication, currently not included in the product labelling.

A 45 year old man with steroid dependent Crohn's disease presented to the outpatient clinic with an acute flare up. At that time he had already been receiving 150 mg of azathioprine and 1000 mg mesalamine by mouth three times a day for about 17 months. Prednisolone had been tapered to 5 mg a day. High resolution intestinal ultrasound showed a subtotal small bowel stenosis. Power Doppler demonstrated mucosal hyperaemia, suggesting an inflammatory process.

It was therefore decided to switch his treatment to infliximab. His condition slightly improved, but after the third course of 5 mg/kg bodyweight infliximab he developed a painful, pustular skin rash on the left side of his chest involving several dermatomas. Varicella zoster IgM titres were raised, confirming an acute shingles infection. He was treated intravenously with 5 mg/kg bodyweight acyclovir every eight hours for seven days. He recovered and was later referred for surgery to resect the inflamed segment.

DISCUSSION

Adult varicella can be a severe illness complicated by pneumonia, encephalitis, hepatitis, thrombocytopenia, and prolonged fever.[3] Blood levels of TNFα have been shown to be raised in patients with acute varicella infection.[4] In vitro studies have shown that replication of varicella zoster virus and varicella zoster virus antigen expression are inhibited by TNFα and that this antiviral activity can be completely blocked by monoclonal antibodies against TNFα.[5]

The use of monoclonal antibodies against TNFα in patients with inflammatory bowel disease increases the risk of viral infections by inhibiting an adequate TNFα response. Doctors should be cautious when prescribing infliximab for patients who are already receiving immunosuppressant drugs. We suggest that varicella zoster virus infection should be included as an infectious complication in the drug labelling.

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