PAPERS AND ORIGINALS

Extra-articular features in early rheumatoid disease

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Summary

One hundred and two patients who presented with rheumatoid disease within the first year of onset were studied prospectively every four months for a mean 4·5 years to assess the incidence of extra-articular features. The features that seemed to be common in the early stages included hand-muscle wasting, carpal tunnel syndrome, lymphadenopathy, non-specific ankle swelling, and rheumatoid nodules, and to a lesser extent hepatomegaly, being underweight, conjunctivitis, skin transparency, and a palpable thyroid gland. Those features which seldom occurred early included scleromalacia, temporal artery involvement, salivary gland enlargement, distal-motor neuropathy, splenomegaly, digital vasculitis, and pulmonary and cardiac complications. Being underweight indicated a significantly more severe outcome.

Introduction

Arthritis may be only one manifestation of rheumatoid disease. This multi-system concept was first advanced in 1948[1] and the term "rheumatoid disease" was subsequently introduced.[2] Since then extra-articular features have been described in many studies, but because of the difficulties of early identification of rheumatoid patients there is little information on the occurrence of extra-articular features within the first few years.

A prospective study of early rheumatoid disease, undertaken at the Middlesex Hospital, has given an opportunity to describe the extra-articular manifestations almost from onset and to assess their significance in relation to other features and to outcome.

Patients and methods

Patients were included in the study if they were referred to the department of rheumatology with a history of polyarthritis of less than one year thought to be due to rheumatoid disease. Those with evidence of psoriatic arthritis, gout, ankylosing spondylitis, Reiter's disease, or colitic arthritis were excluded. The patients attended a special research clinic three times a year. Here they were examined by a trained rheumatologist and the extra-articular features were noted. The rheumatoid status was recorded,[3] the patient was placed in one of four functional grades,[4] the sheep cell agglutination test (SCAT) was performed,[5] and *x*-ray pictures of chest, hands, feet, and cervical spine were taken each year to note joint erosions. Habitus was assessed as weight for height, age, and sex.[6]

One-hundred-and-two patients (44 men, 58 women) were studied. These were followed in the research clinic for 18 months or longer or until death (mean 44 months). Mean delay from the onset of symptoms to the first visit to the research clinic was 7·9 months and the mean duration of disease was 4·5 years. The patients' mean age at onset was 49·2 years (range 19-74 years; peak incidence 55-64 years).

The patients were divided into three prognostic groups according to the course the disease took. This assessment was based on clinical features only. An improved group contained those patients who improved to, or remained in, functional grade I and who had minimal or no residual problems as measured by joint disease, early morning stiffness, or grip strength. A mild group included those who improved to, or remained in, functional grade I, but still suffered mildly from some joint disease, early morning stiffness, or loss of grip strength. The third group contains those whose condition was more severe or deteriorating; these were persistently in functional grade II or worse or suffered persistently from joint disease, early morning stiffness, and loss of grip strength.

The results described here are from the first, fourth, and seventh visits (mean 8, 20, and 32 months from onset) and overall (mean disease duration 4·5 years). The patients analysed at these visits numbered 102, 87, 78, and 102 respectively. The presence of individual extra-articular features at the first visit was correlated with age, sex, functional grade, seropositivity to rheumatoid factor, erosive state, and the prognostic grade described above.

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Results

At the first visit 41 patients (40%) had a positive SCAT result, and the number increased to 67 (66%) at some stage during follow-up. Joint erosions were seen in 25 patients (25%) at the first visit and 70 (69%) overall. At the first visit 48 patients (47%) were in functional grade II or worse, and 70 (69%) had either definite or classical rheumatoid disease.

The extra-articular features assessed and their incidence are shown in table I. The number of patients showing concurrence of different extra-articular features during follow-up is shown in table II. Arthritis was the sole feature of the disease in only eight patients. The others showed at least one other manifestation at some stage.

TABLE I—*Percentages of extra-articular features present at various stages after onset of rheumatoid disease*

Follow-up (months):	8	20	32	Overall
Episcleritis	2	0	3	9
Scleromalacia	0	0	0	4
Conjunctivitis	7	6	3	18
Iritis	0	0	0	2
Tender temporal artery	0	0	0	3
Palpable thyroid	7	7	5	13
Palpable salivary gland	2	0	0	7
Skin transparency	5	3	8	17
Bruising	3	5	1	13
Rheumatoid nodules	12	6	6	31
Hand-muscle wasting	17	25	24	58
Median nerve sensory signs	19	14	12	52
Distal sensory neuropathy	3	2	4	15
Distal motor neuropathy	0	0	0	3
Palpable liver	9	8	2	21
Palpable spleen	0	0	0	2
Palpable lymph nodes	14	8	8	41
Non-specific ankle oedema	12	11	10	31
Vasculitis	0	0	0	1
Underweight	9	9	14	11

TABLE II—*Concurrence of extra-articular features*

No of concurrent features:	0	1	2	3	4	5	6	7	8	9	10
No of patients:	8	13	17	22	9	14	6	4	6	0	3

At the first visit a worse functional grade was associated with the presence of rheumatoid nodules ($P<0.01$), hand-muscle wasting ($P<0.01$), and lymphadenopathy ($P<0.05$). Hepatomegaly was more common in men, eight of the nine patients with hepatomegaly being men. There were no significant associations with age, the presence of rheumatoid factor, or radiological erosions.

The only feature that correlated with outcome was habitus. Patients who were underweight tended to fare worse and patients who were average or overweight had a less severe disease ($r = 0.2$; $P<0.05$).

Overall 26 patients improved, 14 pursued a mild steady course, and 62 pursued a persistently severe or deteriorating course.

Discussion

Our study has shown a high early incidence of extra-articular features in rheumatoid disease with 94 out of 102 patients showing manifestations in the 4·5 years from onset. This was so even though there was no bias towards severity in the sample, which included patients who had possible and probable disease as well as those with definite and classical disease. Only 8% showed no systemic manifestations and 41% had four or more. Gordon *et al*[7] described an inpatient group with definite or classical disease, and, while their study differed from ours, they also showed a high incidence (76%) of extra-articular features. Nevertheless, 58% of their group had none or only one of these features.

The high overall incidence of systemic manifestations that we found may be related to the comprehensive data we obtained by examining the patients systematically every four months. The incidence of symptoms overall was much greater than at any single visit. This suggests the intermittent nature of many of these features and shows the different disease picture seen with close monitoring, in contrast to that seen with isolated assessment of point prevalence.

The two most common features were hand-muscle wasting (17% at the first visit; 58% overall) and evidence of median nerve compression (19% at the first visit; 52% overall). Median nerve compression was not confirmed by conduction studies, but was assessed on the basis of painful paraesthesia in the distribution of the median nerve associated with a positive Tinel sign or diminished two-point discrimination. A mild conjuctivitis was the main eye complication. Only a few patients developed episcleritis; the more serious condition of scleromalacia did not seem to be an early problem. Evidence of reticuloendothelial involvement was obvious from the start, with lymphadenopathy in 14% and hepatomegaly in 9% at the start (41% and 21% overall respectively). Clinical disease of the reticuloendothelial system did not, however, extend to splenomegaly, which was seen in only two patients. These findings differ from those of Gordon *et al*,[7] who studied more severely affected patients later in the course of the disease and observed splenomegaly in 9% but lymphadenopathy in only 12%. Skin manifestations were relatively common in our study, transparency being seen most often. The rheumatoid nodule is obviously not just a later feature of the disease; as many as 12% of our patients were nodular at the first visit and this rose to 31% overall. Eleven per cent of patients were underweight overall, and non-specific ankle oedema also seemed to be an early manifestation; other specific causes of oedema, including gravitational ones, were excluded. One patient developed digital vasculitis, which confirmed that while this is an unusual early complication it is not related only to severe long-standing disease.[8]

Many patients in the study had chronic chest problems, but none was considered a direct complication of rheumatoid disease. Similarly, cardiac problems were not obvious at the research clinic. One patient who died suddenly, however showed gross rheumatoid cardiac involvement at necropsy with multiple nodules in the myocardium and rupture through a softened nodule near the sinus of Valsalva.

In other studies men have had an increased incidence of extra-articular features,[7 9] but we found this with hepatomegaly only. A more severe disease in the first year, as measured by functional grade, was associated with the presence of rheumatoid nodules, hand-muscle wasting, and lymphadenopathy, but the only extra-articular feature at the first visit that showed a relationship to outcome was weight. Being underweight early indicated an eventually more severe disease. In the few other studies in which weight has been assessed this impression has not emerged: weight measurement did not give a guide to outcome,[10] weight loss of more than 4·5 kg did not relate to prognosis,[11] and nutritional impairment was not associated with the development of erosions.[12] Nevertheless, our evidence that being underweight early heralds a more severe form of the disease is a valuable guide to the clinician in predicting outcome.

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Prognostic value of early features in rheumatoid disease

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Summary

Extensive data on 102 patients who presented with rheumatoid disease within a year of onset were gathered by a prospective study to assess the prognostic value of early features. Outcome was evaluated at a mean 4·5 years from onset on the basis of functional grade, extent of joint disease, early morning stiffness, and grip strength. Twenty-six patients improved, 14 pursued a mild steady course, and 62 had a persistently severe or deteriorating condition.

The features recorded at the first visit were correlated with outcome. Those indicating a poor prognosis were: older age at onset, being underweight, poor grip strength, many affected joints, involvement of wrist or metatarsophalangeal joints, poor functional status, fulfilment of many of the American Rheumatism Association criteria for rheumatoid disease, raised erythrocyte sedimentation rate, seropositivity on sheep cell agglutination or latex tests, low haemoglobin level, raised blood urea level, and early erosions on x-ray films.

Introduction

The difficulty of predicting outcome in early rheumatoid disease is well known.[1] [2] The clinician must attempt this, however, as treatment may necessitate the use of hazardous drugs best not given if remission is likely. The relation of early features to the subsequent course is therefore of great practical importance. A recent prospective study of early rheumatoid disease undertaken at the Middlesex Hospital has provided an opportunity to record the features of the disease almost from onset, to relate these to outcome, and to assess their prognostic significance.

Patients and methods

The design of this study has been described.[3] Altogether 44 men and 58 women were studied. This near equal representation of the sexes has been seen in other studies dealing exclusively with early rheumatoid disease.[4] Ten patients died during the study. Their mean age at death was 64·7 years. Three died before completing 18 months' follow-up: two men in their late 60s with nodular rheumatoid disease, one of whom had right bundle branch block, died from bronchopneumonia secondary to long-standing bronchitis and emphysema; the woman committed suicide. For prognostic purposes all three were included in the severe group. Of the other seven who died only one woman, who died at the age of 49, was thought to have died of rheumatoid disease. She was known to have atrioventricular heart block, and the necropsy showed rheumatoid nodules in the conducting tissue of the heart, the endocardium of the right ventricle, and in both lungs. Two patients died from bronchopneumonia, one after a stroke, one from senile dementia after a long period in hospital, one from chronic congestive heart failure, and one from metastases after excision of a colonic carcinoma. All 10 patients who died were included in the analysis.

The patients were divided into three prognostic groups according to the course the disease had taken. This assessment was based on clinical features only, including functional grade, extent of joint disease, early morning stiffness, and grip strength. Twenty-six patients improved, 14 pursued a mild steady course, and 62 had a persistently severe or deteriorating condition.

Data from the research clinics were transferred to 80-column punch cards for subsequent analysis. All the variables recorded at the first visit with a frequency of at least 15% were correlated with the above prognostic gradings to identify the variables with prognostic value. Analysis involved rank-order correlation, with pair-wise deletion of missing values, obtaining Spearman's r_s, adjusted for tied ranks, as the correlation coefficient.

Results

The variables associated with prognosis are summarised in the table.

Early features indicating prognosis

Variables	Significance	
	r_s	P
Age	0·2280	0·05
Grip strength	0·3077	0·005
No of joints affected	0·2938	0·005
Body habitus	0·1992	0·05
Wrist involvement	0·2406	0·05
MTP joint involvement	0.2234	0·05
Functional status	0·2806	0·005
No of American Rheumatism Association criteria fulfilled	0·2389	0·05
ESR	0·3693	0·001
Haemoglobin level	0·2629	0·01
Blood urea level	0·2028	0·05
Rheumatoid factor:		
Latex test	0·4102	0·001
SCAT	0·4078	0·001
Joint erosions	0·2206	0·05

Age and sex—Age was closely associated with outcome, with older patients having a more severe form of the disease. Sex showed no such association.

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