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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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Social and historical features—Variables in this group were: social grade; adverse social factors relating to finance, housing, work, and interpersonal relationships; number of children; age at menopause; personal history; family history of rheumatoid disease; prodromata; precipitating factors; time-lag to presentation. None was associated with prognosis.

Joint features—This group of variables concerned actual joint disease in the early stages: type and site of onset, symmetry at onset, subsequent symmetry, extent of joint involvement, grip strength, presence of erosions on *x*-ray films, and early hospital admission. Three variables had prognostic value. Severe disease was associated with more clinically affected joints, weak grip strength, and early presence of erosions on *x*-ray films.

Particular site of joint disease—Of the particular sites of clinical joint disease (swelling, tenderness, or pain on movement) seen at the first clinic visit, an arthritis of both wrists or of the right metatarsophalangeal (MTP) joints heralded a more severe disease.

Extra-articular features—Those extra-articular features that were common enough at the first visit to warrant analysis were hand muscle wasting, median nerve sensory signs, lymphadenopathy, early morning stiffness, and body habitus. Of these habitus showed prognostic value, with those who were underweight for height, age, and sex[5] eventually developing a more severe disease.

Laboratory measurements—Investigations performed at the first visit included measurements of haemoglobin level, white cell count, platelet count, erythrocyte sedimentation rate (ESR), blood urea level, serum protein concentrations, rheumatoid factor by sheep cell agglutination test (SCAT) and latex test, anti-nuclear antibody, and antithyroid antibodies. A worse outcome was associated with a low haemoglobin level, a raised ESR, a raised blood urea level (above 6·5 mmol/l (39 mg/100 ml), and both the presence and titre of rheumatoid factor.

Discussion

Many published reports on prognosis in rheumatoid disease are contradictory. New evidence mainly simply endorses or refutes previous work. Thus our finding that an early poor functional grade indicates a bad prognosis agrees substantially with those of others,[4 6 7] while our evidence that sex does not prejudice outcome disagrees with findings in other studies, which suggest that men, at least in the early stages, fare better.[8–13] Many of these reports are of selected and heterogeneous samples studied retrospectively and at different times from onset, however; of more interest are those which have based their prognoses on observations of early rheumatoid disease.

Otten and Boerma,[9] reporting on 141 patients seen within six months of onset, found that a good prognosis was indicated by short disease duration before presentation, male sex, and absence of rheumatoid factor. Jacoby *et al*[4] studied 100 patients seen within one year of onset and suggested that a more severe outcome was associated with a low haemoglobin level, poor functional capacity, and raised rheumatoid factor titre. Two hundred and fifty patients followed for 10 years by Bywaters[14] included 125 seen within one year of onset. A better prognossis was noted with male sex, younger age, asymmetric joint disease, fewer affected joints, associated psoriasis, and absence of rheumatoid factor. Wawrzynska-Pagowska *et al*[15] studied 202 pre-erosive cases (although only 30 had had disease for under a year) and found that progression to erosions was associated with subcutaneous nodules, hand muscle atrophy, lymphadenopathy, seropositivity, anaemia, presence of c-reactive protein, insidious onset, and disease of only hands or feet, or both, at onset.

Our results show clearly that older patients tend to fare worse than younger ones. In an aging population even a modest early loss of function may affect patients more.

Social factors were investigated by Duthie *et al.*[8 16] They reported that the lower economic classes tended to fare better in the early stages; that clinical improvement could be affected by the social situation, unskilled labourers faring worse in this respect; that an overall poor prognosis could be associated with adverse domestic and financial circumstances; and that final functional capacity was closely related to the frequency of unresolved social problems. We could not confirm an early association of social status and social factors with prognosis.

Like Jacoby *et al*[4] and Short *et al*[17] we found that patients with a family history of rheumatoid disease can be reassured that they are no more likely than others to do badly.

There is a strong impression that a good prognosis is associated with short disease duration before presentation[9 18–21] and with early hospital admission,[10 11 16] but we could not confirm this. Forty-three of our patients presented within three months of the onset of symptoms and they fared no differently from the remainder of the group. Furthermore, 35 patients were admitted to hospital within the first two years of onset. They were certainly no better off than the others and might just have been worse ($P < 0{\cdot}1$). Jacoby *et al*[4] found that early hospital admission did not improve their patients' chances. This is not surprising, as patients with the severest disease are more likely to receive inpatient treatment. Patients who are admitted earlier may do better than those admitted later, but our impression is that if they have to be admitted at all they have more severe disease, which tends to persist.

Although some have disagreed,[4 11] the type of onset is generally considered to influence prognosis, the acute type being related to a better prognosis and longer remissions and the insidious type to a worse prognosis.[8 13 15 21] We found a strong indication that those with an insidious onset tend to fare worse. Furthermore, three patients with a palindromic onset also pursued a severe course.

Occasional conflicting reports have related the symmetry of joint disease, whether at onset or later in the disease, to prognosis.[11 12 15 20] In our study symmetry of joint disease at onset had no predictive value, but progression to symmetry within the first year did. We think ($P = 0{\cdot}06$) that the asymmetric form may be less severe.

Few workers have suggested that a particular site of early joint disease is of prognostic significance.[9 20] We could not show that the site of disease at onset was predictive, but clearly subsequent early wrist and MTP joint disease carried a worse prognosis. Nine well-defined patterns of disease were revealed by factor analysis,[22] including one based on wrist, elbow, shoulder, and knee and one based on MTP joints I and II. These patterns indicated a poorer prognosis.

Body habitus was the only extra-articular feature with predictive value; being underweight indicated a more severe form of the disease. We have already discussed this finding,[3] which has not been shown in other studies.[11 15 20] Subcutaneous rheumatoid nodules are considered indicative of potentially severe disease. Their incidence in this study was not high enough for useful analysis, but, surprisingly, the 12 patients who did show them at the first visit appeared to fare no worse than the others.

The rheumatoid factor again emerged with strong predictive value, confirming the evidence since the introduction of tests for rheumatoid factor that both presence and titre are ominous. An unexpected early increase in the blood urea level was found in 22 patients, who subsequently developed a more severe disease.

Problems of sampling arise in identifying and following patients with early rheumatoid disease, and some studies tend to regard hospital-derived samples as representative of the condition. The results presented here cannot be true for all people with rheumatoid disease, so the usefulness of our generalisations is limited. But as there is still no distinct, historical, clinical, or laboratory discriminator for severity in the practical task of predicting outcome the clinician must use what is available. If the features identified here are carefully observed and used together they may prove of value in the prognostic assessment of the patient with early rheumatoid disease.

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Group B streptococci in the female genital tract

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Summary

Vaginal carriage rates of group B streptococci among 250 women attending a clinic for sexually transmitted diseases, 123 attending family planning clinics, and 110 in labour were 36·0%, 17·1%, and 6·4% respectively. The presence of group B streptococci was not associated with a vaginal discharge or the use of oral contraceptives in the non-pregnant women, or with the isolation of Neisseria gonorrhoeae or Trichomonas vaginalis from the women attending the clinic for sexually transmitted diseases. Serotyping showed a predominance of types II and III in non-pregnant women and an overall incidence of non-typable strains of 14·8%. There was no relationship between serotype and antibacterial susceptibility.

Introduction

Group B streptococci (*Streptococcus agalactiae*) are increasingly being recognised as a cause of serious perinatal infection, producing meningitis, septicaemia, or a fulminating pneumonitis, and as being associated with high mortality and morbidity rates.[1-9] Studies have shown the importance of transmission from mother to infant either in utero or during parturition,[2-4 10] although the possibility of nosocomially acquired infection from attendants[11] has not been entirely excluded. There is also evidence that sexual transmission may be important.[1 12]

To try to establish the degree of risk of infection to the neonate and to examine the possibility of venereal transmission we assessed the vaginal carriage rates of group B streptococci in three categories of women: women in labour, women attending a clinic for sexually transmitted diseases (STD clinic), and women attending family planning clinics. In addition, all isolates were serotyped and their susceptibilities to various antibacterial agents determined.

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Patients and methods

The three categories of women were made up as follows: category 1, 110 women in labour, with intact membranes, admitted non-consecutively to the maternity department of St Thomas's Hospital; category 2, 123 women attending either of two family planning clinics, one at the Lambeth Hospital, London, and the other at a general practitioner clinic in Farnborough; and category 3, 250 non-pregnant, premenopausal women attending non-consecutively and for the first time the STD clinic at St Thomas's Hospital. Details on vaginal discharge and the use of oral contraceptives were obtained from women in categories 2 and 3, those in category 3 being examined for sexually transmitted diseases after the study sample had been obtained.

Under direct vision high vaginal samples were obtained on charcoal-impregnated swabs from the posterior or lateral fornices. No antibacterial or lubricating creams were used. The swabs were placed in Stuart's transport medium and processed within 16 hours by plating on Oxoid Columbia agar (Oxoid CM 331) containing 6% horse blood, and on blood agar containing 0·0002% crystal violet and 0·08% chloral hydrate. The swabs were then placed in a liquid selective culture medium containing 5 ml Todd-Hewitt broth—8 mg gentamicin and 15 mg nalidixic acid per l—and incubated for 18 hours at 37°C in 10% CO_2. Subcultures were made from this medium to Columbia blood agar. All plates were incubated for 18 hours at 37°C in 10% CO_2 and examined for β-haemolytic colonies, which were then stained by Gram's method. All streptococcal isolates that failed to hydrolyse aesculin and ferment mannitol were then grouped by Lancefield's acid extraction method.[13] Isolates of group B streptococci were serotyped at the Streptococcus Reference Laboratory, Colindale.

Finally, all isolates were examined for their susceptibility to benzylpenicillin, ampicillin, tetracycline, erythromycin, clindamycin, trimethoprim, sulphamethoxazole, gentamicin, and kanamycin by determining the minimum inhibitory concentrations (MICs). An inoculum of 10 000 colony-forming units was used on diagnostic sensitivity test agar (Oxoid CM 261) containing 6% lysed horse blood and appropriate concentrations of antibacterials and incubated aerobically for 18 hours at 37°C. MICs were read as the smallest amount of antibacterial producing complete or almost complete inhibition of growth.

Results

Table I shows the isolation rates of group B streptococci in the three categories of women. There was no statistically significant association between the presence of group B streptococci and either a vaginal discharge or the use of oral contraceptives in categories 2 and 3, or the isolation of *Neisseria gonorrhoeae* or *Trichomonas vaginalis* in category 3.