LIVER PALMS IN RHEUMATOID ARTHRITIS

BY

B. McAVOY, K. WHALEY, G. NUKI, W. CARSON DICK,
AND W. WILSON DOWNIE

*From the Centre for Rheumatic Diseases, Glasgow, and the University Department of Medicine,
the Royal Infirmary, Glasgow, C.4*

Liver palms or palmar erythema are well recognized as a clinical feature of hepato-cellular disease (Sherlock, 1968). They have also been recorded in many other conditions, such as pregnancy, chronic febrile states, leukaemia, thyrotoxicosis, and rheumatoid arthritis (Copeman, 1964; Ragan, 1966; Sherlock, 1968). In the last-named disease the prevalence of palmar erythema has not been, to our knowledge, ascertained. In this paper we report a study of palmar erythema in 144 patients with rheumatoid arthritis, in whom we have studied the relationship of palmar erythema to the clinical and laboratory features of the disease.

Material and Methods

Patients

A series of 144 patients with probable, definite, or classical rheumatoid arthritis as defined by the diagnostic criteria of the American Rheumatism Association (Ropes, Bennett, Cobb, Jacox, and Jessar, 1959) was studied. There were 97 females (mean age 50.2 years, range 16 to 75) and 47 males (mean age 55.5 years, range 19 to 70).

A further series of 144 hospital patients matched for age and sex with the rheumatoid patients served as controls. None of these had rheumatoid arthritis or any other disease associated with palmar erythema (Sherlock, 1968).

Liver Palms

Palmar erythema was recorded as absent (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Observations were all made in hospital, where the environmental temperature was approximately 21°C. The palms were also recorded as being either hot or cold.

The inter-observer and intra-observer variations in interpreting palmar erythema were studied. Table I (opposite) shows the differences recorded between three observers (B, C, and D) and a standard observer (A) for the four grades of palmar erythema. There is consider-

able inter-observer variation. The concordance rate for the three observers with the standard observer was:

B versus A	62.5 per cent.
C versus A	66.7 per cent.
D versus A	64.4 per cent.

B was discordant with A in one grade of palmar erythema in 30.0 per cent. of cases, and in two grades in 7.5 per cent.

C was discordant with A in one grade of palmar erythema in 27.9 per cent. of cases, in two grades in 4.2 per cent. and in three grades in 0.2 per cent.

D was discordant with A in one grade of palmar erythema in 24.4 per cent. of cases, and in two grades in 11.2 per cent.

The discordance between B and A, C and A, and D and A for grade 0 versus 1, 2, or 3 were 30.0, 18.8, and 13.4 per cent. respectively.

That these differences were not accounted for by errors of assessment by A was shown by the almost identical results when B was compared with another observer E in a further series of 27 patients:

Overall concordance	63.0 per cent.
Discordance in one grade	37.0 per cent.
Discordance in grade 0 versus 1, 2, or 3	22.2 per cent.

When, however, B was compared to observer F, who had severe red-green colour-blindness, in the same 27 patients, the variation was even higher:

Overall concordance	44.4 per cent.
Discordance in one grade	40.7 per cent.
Discordance in two or three grades	14.9 per cent.
Discordance in grade 0 versus 1, 2, or 3,	44.4 per cent.

To determine the intra-observer variation, one of us (Observer A) examined 150 patients twice within 30 minutes under identical conditions (Table I). The overall concordance was 74.3 per cent. and the discordance in one grade was 25.7 per cent. No discord-

TABLE I
INTER- AND INTRA-OBSERVER VARIATIONS IN GRADING PALMAR ERYTHEMA

Comparisons		B v. A	C v. A	D v. A	A v. A
GRADE 0	Concordant	15	28	27	80
	Discordant by 1 grade	10	2	1	12
	Discordant by 2 grades	1	0	2	0
	Discordant by 3 grades	0	0	0	0
GRADE 1	Concordant	2	2	1	15
	Discordant by 1 grade	1	6	5	17
	Discordant by 2 grades	1	1	0	0
GRADE 2	Concordant	3	2	0	9
	Discordant by 1 grade	1	4	4	7
	Discordant by 2 grades	1	0	2	0
GRADE 3	Concordant	5	0	1	8
	Discordant by 1 grade	0	1	1	2
	Discordant by 2 grades	0	1	1	0
	Discordant by 3 grades	0	1	0	0
Overall Concordance (per cent.)		62.5	66.7	64.4	74.3
Discordant by 1 grade (per cent.)		30.0	27.9	24.4	25.7
Discordant by 2 grades (per cent.)		7.5	4.2	11.2	0
Discordant by 3 grades (per cent.)		0	0.2	0	0
Discordant grade 0 versus 1 + 2 + 3 (per cent.)		30	18.8	13.4	16.8

ance was noted by more than one grade. The discordance between grade 0 versus 1, 2, or 3, was 16.8 per cent. This was entirely due to differences in differentiating grades 0 and 1.

Because of the relatively large disagreement in interpreting palmar erythema between different observers, one observer (A) made all the observations.

Other Clinical and Laboratory Data

In addition to the age and sex of the patient and the presence of palmar erythema, the following clinical facts were recorded: duration of arthritis, presence of subcutaneous nodules, articular index (Ritchie, Boyle, McInnes, Jasani, Dalakos, Grievson, and Buchanan, 1968), and functional grade (Steinbrocker, Traeger, and Batterman, 1949). Laboratory investigations included: x-ray stage (Steinbrocker, Traeger, and Batterman 1949), sheep cell agglutination test for rheumatoid factor (Ziff, Brown, Lospalluto, Badin and McEwen 1956), and a test for antinuclear factor using the indirect immunofluorescence method of Beck (1961).

Results

These are shown in Tables II and III (overleaf).

The prevalence of palmar erythema in male and female patients with rheumatoid arthritis is shown in Table II. It can be seen that the prevalence and the distribution of the grades of palmar erythema in the female rheumatoid patients and the female controls is almost identical. However, the male patients with rheumatoid arthritis show a higher prevalence of Grades 2 and 3 palmar erythema (23.4 per cent.) compared with the male controls (4.2 per cent.). This difference is significant ($\chi^2 = 5.7132$; $P < 0.025$, using Yate's correction for small numbers).

It is noteworthy that the female controls had a significantly higher prevalence of Grades 2 and 3 palmar erythema (17.5 per cent.) than the male controls (4.2 per cent.) ($\chi^2 = 3.7782$; $P < 0.05$ with Yate's correction for small numbers).

No differences were noted in mean age and age distribution of the male or female rheumatoid patients with palmar erythema compared with the control patients who also had palmar erythema. Thus, the mean age of the female rheumatoid patients with palmar erythema of all grades (1, 2, and 3) was 52.5 years (S.D. ± 13.3) and that of the female controls was 52.3 years (S.D. ± 13.6). The mean age of the male rheumatoid patients with palmar erythema of all grades was 58.2 years (S.D. ± 8.9) and that of the male controls 59.2 years (S.D. ± 8.7).

The relation of palmar erythema to the clinical and laboratory features of the rheumatoid patients is shown in Table III. When patients with Grade 0 are compared to patients with Grades 1, 2, and 3 palmar erythema, those with Grades 1, 2, and 3 have a longer duration ($t = 2.0864$; $P < 0.05$) and more severe arthritis, as shown by a higher articular index ($t = 1.8008$; $P < 0.05$) and higher functional class ($\chi^2 = 4.4703$; $P < 0.05$). Patients with Grades 1, 2, and 3 included a significantly higher number with positive antinuclear factor tests ($\chi^2 = 3.8412$; $P < 0.05$).

When patients with Grade 0 are compared with patients with Grades 2 and 3, the latter tend to be older ($t = 2.8967$; $P < 0.005$) and to have had arthritis for a longer time ($t = 3.5910$; $P < 0.001$). They also tend to have more severe disease, as judged by an increased prevalence of subcutaneous

TABLE II
A COMPARISON OF THE GRADES OF PALMAR ERYTHEMA: PATIENTS WITH RHEUMATOID ARTHRITIS WITH AN AGE AND SEX-MATCHED CONTROL POPULATION IN MALES AND FEMALES

Sex	Age (yrs)	Rheumatoid Arthritis								Controls							
		Grade 0		Grade 1		Grade 2		Grade 3		Grade 0		Grade 1		Grade 2		Grade 3	
		No.	per cent.	No.	per cent.	No.	per cent.	No.	per cent.	No.	per cent.	No.	per cent.	No.	per cent.	No.	per cent.
Female	0-20	2	(2.1)	1	(1.0)	0		0		2	(2.1)	1	(1.0)	0		0	
	21-40	13	(13.4)	4	(4.0)	2	(2.1)	1	(1.0)	13	(13.4)	2	(2.1)	3	(3.1)	2	(2.1)
	41-60	23	(23.7)	13	(13.4)	7	(7.2)	5	(5.2)	26	(26.8)	15	(15.5)	3	(3.1)	4	(4.1)
	61-80	14	(14.4)	7	(7.2)	3	(3.1)	2	(2.1)	12	(12.3)	9	(9.2)	2	(2.1)	3	(3.1)
	Total	52	(53.6)	25	(25.8)	12	(12.3)	8	(8.3)	53	(54.6)	27	(27.8)	8	(8.3)	9	(9.3)
Male	0-20	0		0		0		0		0		0		0		0	
	21-40	2	(4.3)	2	(4.3)	0		0		4	(8.5)	0		0		0	
	41-60	16	(4.0)	4	(8.5)	3	(6.4)	3	(6.4)	19	(40.4)	6	(12.8)	0		1	(2.1)
	61-80	7	(14.8)	5	(10.6)	3	(6.4)	2	(4.3)	9	(19.1)	7	(14.8)	1	(2.1)	0	
	Total	25	(53.2)	11	(23.4)	6	(12.8)	5	(10.6)	32	(68.1)	13	(27.7)	1	(2.1)	1	(2.1)

TABLE III
RELATION BETWEEN GRADES OF PALMAR ERYTHEMA AND CLINICAL AND LABORATORY FEATURES OF THE DISEASE

Clinical and Laboratory Features	Grade of Palmar Erythema		
	Grade 0 (n = 76)	Grade 1 + 2 + 3 (n = 64)	Grades 2 + 3 (n = 29)
Age (yrs) Mean $\pm$ S.D.	50.07 $\pm$ 12.80	53.98 $\pm$ 12.23	56.17 $\pm$ 8.31
Sex Female	54 (71.1%)	42 (65.6%)	18 (62.1%)
Male	22 (28.9%)	22 (34.4%)	11 (37.9%)
Duration of Disease (yrs) Mean $\pm$ S.D.	7.96 $\pm$ 9.32	11.34 $\pm$ 9.69	15.95 $\pm$ 10.51
Subcutaneous Nodules	18 (23.7%)	20 (31.3%)	11 (37.9%)
Rheumatoid Factor (Sheep cell agglutination test > 1/32)	55 (72.4%)	50 (78.1%)	25 (86.2%)
Antinuclear Factor (> 1/16)	17 (22.4%)	24 (37.5%)	12 (41.4%)
X-Ray Stage I + II	24 (31.6%)	12 (18.8%)	2 (6.9%)
III + IV	52 (68.4%)	52 (81.2%)	27 (93.1%)
Functional Grade I + II	48 (63.2%)	29 (45.3%)	14 (48.3%)
III + IV	28 (36.8%)	35 (54.7%)	15 (51.7%)
Articular Index: Mean $\pm$ S.D.	20.63 $\pm$ 15.17	26.00 $\pm$ 17.23	24.04 $\pm$ 15.90

nodules, positive tests for rheumatoid and antinuclear factors, more severe radiological involvement, lower functional grade, and higher articular index. However, only in the case of the antinuclear factor ($\chi^2 = 3.7948$; $P < 0.05$) and X-ray stage ($\chi^2 = 6.8640$; $P < 0.01$) were these differences of statistical significance.

Discussion

It is essential when evaluating a clinical sign in medicine to determine the inter- and intra-observer error in the interpretation of the sign. In this study we have defined three grades of palmar erythema, mild (+1), moderate (+2), and severe (+3). In an inter-observer error study we found an overall concordance in interpretation of the grades of palmar erythema of 62.5 to 67.7 per cent. Variations of one grade of palmar erythema were frequent, and

differences were observed even with the severer grades. Considerable differences were observed when a physician, who was severely red-green colour blind, was compared with other physicians with normal colour vision. When one observer's own successive results were compared the overall concordance rate was somewhat improved (74.3 per cent.), and his findings were discordant by only one grade. Because of the relatively high inter-observer error, one physician made all the observations used in this study. Similar observer differences have been noted in assessing cyanosis (Comroe and Botelho, 1947), joint inflammation (O'Sullivan, Cathcart, and Bolzan, 1968; Ritchie and others, 1968), goitre size (Crooks, Aboul-Khair, Turnbull, and Hytten, 1964), physical signs in the chest (Fletcher, 1952; Schilling, Hughes, and Dingwall-Fordyce, 1955; Fletcher and Oldham, 1964), neuro-

logical signs (Kuzma, Tourtellotte, and Remington, 1965), chest x-rays (Birkelo, Chamberlain, Phelps, Schools, Zacks, and Yerushalmy, 1947), x rays of the hands in rheumatoid arthritis (Kellgren, 1956), and electrocardiograms (Davies, 1958).

The finding of palmar erythema in rheumatoid arthritis is somewhat dubious, for no significant difference was noted in the prevalence of palmar erythema (of all grades) in female rheumatoid arthritic patients and in controls matched for age and sex (Table II). In male rheumatoid patients there was, however, a significantly higher prevalence of palmar erythema of more severe degree (Grades 2 and 3) than in the male controls. The absence of any difference between female rheumatoid patients and female controls may be related to the higher prevalence of palmar erythema in the female controls compared with the male controls. All the patients were examined in the same environmental conditions, and the prevalence of cold palms was the same in all groups. The mean age of female and male rheumatoid patients with palmar erythema was the same as that of female and male controls with palmar erythema.

The rheumatoid patients with palmar erythema tended to be slightly older, to have a longer duration of arthritis, and to have more severe arthritis than patients who had no palmar erythema.

This study has demonstrated that there is a high

inter-observer error in interpreting and grading palmar erythema, and that when properly age and sex-matched controls are studied it is possible to show a significant increase of palmar erythema only in male patients with rheumatoid arthritis. The sign is therefore of limited clinical importance.

Summary

The prevalence of liver palms or palmar erythema in 97 female and 47 male patients with rheumatoid arthritis was compared to the prevalence in a control series of 97 age-matched females and 47 age-matched males. Liver palms were found with equal frequency in the female rheumatoid subjects and the female controls. There were more liver palms in the male rheumatoid patients than in the male controls. Liver palms tended to occur in those patients whose arthritis was of longest duration and greatest severity. Because of the high inter-observer error in interpreting liver palms, it is concluded that this physical sign is of relatively little importance.

The authors wish to thank Dr. W. Watson Buchanan for helpful criticism and advice. The study was supported by a grant from the Arthritis and Rheumatism Council for Research in Great Britain. One of us (G.N.) was in receipt of a CIBA clinical research fellowship.

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L'érythème palmaire dans la polyarthrite rhumatoïde

RÉSUMÉ

La distribution de l'érythème palmaire chez 97 femmes et 47 hommes atteints de polyarthrite rhumatoïde a été comparée à la distribution chez un groupe de 97 femmes et 47 hommes témoins d'âge comparable. L'érythème palmaire a été vu avec la même fréquence chez les femmes atteintes de polyarthrite rhumatoïde que chez les femmes témoins. Il y avait plus de cas d'érythème palmaire chez les hommes atteints d'arthrite rhumatoïde que chez les hommes témoins. L'érythème palmaire avait tendance à se présenter chez les malades dont l'arthrite durait depuis longtemps et était plus sévère. A cause de la grande erreur en interprétant l'érythème palmaire par les différents observateurs, on conclut que ce signe clinique n'est que d'une importance relativement minime.

Palmas hepáticas en la poliartritis reumatoide

SUMARIO

La presencia de palmas hepáticas o eritema palmar en 97 pacientes mujeres y 47 hombres con poliartritis reumatoide fue comparada con la frecuencia en una serie de testigos de la misma edad, compuesta por 97 mujeres y 47 hombres. Se descubrieron palmas hepáticas con igual frecuencia en los sujetos reumatoides femeninos y en las mujeres testigo. Había más palmas hepáticas en los pacientes reumatoides maculinos que en los hombres testigo. La eritema palmar tendía a ocurrir en aquellos pacientes cuya artritis era más antigua y de mayor severidad. A causa del alto grado de error entre observadores al interpretar la palma hepática, se llega a la conclusión de que esta manifestación física es de relativamente poca importancia.