RAYNAUD'S PHENOMENON IN RHEUMATOID ARTHRITIS

A. SARAUX, J. ALLAIN, C. GUEDES, D. BARON, P. YOUINOU* and P. LE GOFF

Unit of Rheumatology and *Laboratory of Immunology, Brest University Medical School Hospital, Brest, 5 avenue Foch, 29200 Brest, France

SUMMARY

The aim of this study was to evaluate the prevalence of Raynaud's phenomenon in patients with rheumatoid arthritis (RA), and to relate this symptom to clinical, radiological and serological characteristics of the patients. All relevant information was retrospectively obtained from the standardized clinical records of 322 RA in-patients first admitted to the Rheumatology Unit of Brest University Medical School Hospital. Raynaud's phenomenon was found in 54 (17.2%) of 322 RA patients. There was no significant correlation between demographic, clinical or radiological characteristics. However, the subgroup of RA patients with Raynaud's phenomenon had a slightly higher prevalence of vasculitis than the subgroup without Raynaud's phenomenon. CRP level and C4 level were found to be lower in the former than in the latter group, whereas ESR and various serological findings (rheumatoid factor, antinuclear antibodies) were comparable in the two groups. We conclude that the prevalence of Raynaud's phenomenon is high in French RA in-patients, and that some clinical and biological abnormalities (vasculitis, low CRP level and low C4 level) suggest an association between Raynaud's phenomenon and vasculitis in a few cases, whereas this association might be fortuitous in the remainder.

KEY WORDS: Raynaud's phenomenon, Rheumatoid arthritis.

The prevalence of Raynaud's phenomenon in rheumatoid arthritis (RA) is not well defined. Following the report by Short et al. [1] of a 10% incidence of vascular spasm in RA, there has been a belief that the association of Raynaud's syndrome with RA is not uncommon. However, Carroll et al. [2] and Grassi et al. [3] did not find a higher prevalence of Raynaud's phenomenon in patients with RA than in those with osteoarthritis. Nevertheless, Drosos et al. [4] found that Greek RA patients had Raynaud's phenomenon more often than British RA patients, and suggested that genetic and environmental factors may be responsible for these differences in disease expression between European populations with RA. The aim of this study was, therefore, 2-fold: to assess the prevalence of Raynaud's phenomenon in a group of in-patients with RA, and to compare the clinical, radiological and serological expression of RA with and without Raynaud's phenomenon.

PATIENTS AND METHODS

Patients

We conducted a retrospective review of the medical charts of 322 RA in-patients admitted for the first time to the Rheumatology Unit of the Brest University Medical School Hospital from 1 January 1981 to 31 December 1994. All met the 1987 ACR revised criteria for RA [5]. None showed features of 'scleroderma spectrum disorders' or systemic lupus erythematosus.

The clinical data (Raynaud's phenomenon, vasculitis, nodules) were collected by physicians, who used a standard form, and had to be recorded even if negative. Each patient had a standard evaluation, including laboratory tests [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF) and antinuclear antibodies (ANA)] and roentgenograms (hands, feet, pelvis, lumbar spine and painful joints).

Methods

Raynaud's phenomenon was defined as episodic well-demarcated pallor and/or cyanosis in response to cold or emotional stress that was relieved by rewarming. The disease activity was evaluated clinically by Ritchie's [6] and Lee's [7] indices.

We reviewed the X-rays of 122 patients taken at random within the first population of patients. Articular damage to the hands was scored according to the method of Steinbrocker, on a scale of 1-4 [8]. RF were measured by the latex test (Biolyon, Paris, France). A positive value for this assay was considered to be a titre >1/40. ANA were tested by indirect immunofluorescence (IIF) on HEp 2 cells as substrate and a titre of at least 1/100 was considered positive. When the ANA were positive, anti-DNA antibodies were determined on Crithidia luciliae.

Data were analysed using the $\chi^2$ test (or Fisher's exact test where appropriate), and by the Kruskal–Wallis $H$-test.

RESULTS

Prevalence of Raynaud's phenomenon

The prevalence of Raynaud's phenomenon and demographic characteristics of the subjects studied are shown in Table I. Raynaud's phenomenon was found in 55 (17.1%) of 322 RA in-patients at their first hospitalization.

Clinical findings

The sex ratio, age and disease duration did not differ significantly between the patients with and
without Raynaud's phenomenon. Neither was there any significant difference between the clinical findings of those who had Raynaud's phenomenon and those who did not. However, 3 (5.4%) of 55 patients with Raynaud's phenomenon compared with 3 (1.1%) of 267 patients without Raynaud's phenomenon had vasculitis including nailfold infarcts ($P = 0.06$).

**Serological findings**

CRP levels were significantly lower in RA patients with Raynaud's phenomenon than in RA patients without Raynaud's phenomenon, whereas ESR and fibrin levels were comparable in the two groups. The C4 level is also lower in the former group than in the latter. Conversely, RF and ANA were comparable in the two groups. None of the patients with Raynaud's phenomenon and ANA had anti-DNA antibodies.

**Radiological findings**

Articular damage to the wrist, metacarpophalangeal joint and proximal interphalangeal joints was, respectively, $2.05 \pm 1$, $1.71 \pm 0.5$ and $1.5 \pm 0.67$ in RA patients with Raynaud's phenomenon and $2.08 \pm 1$, $1.71 \pm 0.92$ and $1.62 \pm 0.82$ in RA patients without Raynaud's phenomenon. The radiological scores did not differ significantly between the two subgroups of patients.

**DISCUSSION**

As reported previously by Drevet et al. [9], we found a high prevalence of Raynaud's phenomenon in French RA patients (17.2%), whereas others reported a low prevalence of Raynaud's phenomenon in other populations of such patients [2, 3]. These discrepancies are probably to be attributed to differences in study design and in study population, and also to differences in the diagnostic criteria for Raynaud's phenomenon. Moreover, Raynaud's phenomenon is not a straightforward diagnosis and a clear history is difficult to elicit, and it has been reported to occur in some 10% of the population [10], especially in young women.

The significance of Raynaud's phenomenon remains unclear in RA patients, and our study was designed to establish whether there are differences between the clinical, laboratory and radiological features and the presence or absence of Raynaud's phenomenon according to our definition. There were no significant differences between the demographic, clinical or radiological findings in the patients with and without Raynaud's phenomenon. However, the subgroup with Raynaud's phenomenon showed a higher prevalence of vasculitis (although not significant) than the subgroup without Raynaud's phenomenon. Similarly, we found a low C4 level in the subgroup with Raynaud's phenomenon, whereas various serological findings (RF, ANA) were comparable in the two groups. These results might be due to the higher prevalence of vasculitis in this group than in the subgroup of RA patients without Raynaud's phenomenon.

Surprisingly, the level of CRP was significantly lower in RA patients with Raynaud's phenomenon than in the other RA patients, while the value of ESR was not significantly different between the two subgroups. We found previously that the CRP response was markedly elevated in patients with at least one extra-articular manifestation, except Raynaud's phenomenon. A number of reports have indicated that most patients with RA have an elevated CRP level in their sera, whereas most of the patients with primary Sjögren's syndrome and systemic lupus erythematosus do not have an elevated CRP level [11]. These results suggest that the presence or absence of Raynaud's phenomenon separates RA patients into two subgroups with different levels of acute-phase reactants.

Thus, Raynaud's phenomenon is common in the general population, but may also be a sign of connective tissue disease. It is present in >90% of patients with scleroderma and in ~20% with systemic lupus erythematosus, Sjögren's disease and dermatomyositis; we found a prevalence of 17% in RA patients and this result suggests that Raynaud's phenomenon is associated with RA. Furthermore, the dermal microcirculatory abnormalities found in RA using periungual capillaroscopy by others [9, 10], the slight association of Raynaud's phenomenon with vasculitis and low C4 level found in this study, are in accord with this conclusion.

We conclude that the prevalence of Raynaud's phenomenon is high in French RA in-patients, and that some clinical and biological abnormalities (vasculitis, low CRP level and low C4 level) suggest an association between Raynaud's phenomenon and vasculitis in a few cases, whereas this association might be fortuitous in the remainder.

**TABLE I**

| Demographic characteristics, clinical and biological features of 322 RA patients with and without Raynaud's phenomenon |
|---|---|---|---|
| **RA patients with Raynaud's phenomenon** | **RA patients without Raynaud's phenomenon** | **P** |
| Total number | 55 | 267 |  
| Sex ratio | 45:10 | 209:58 | NS |
| Age | 57.9 ± 13.4 | 58.4 ± 14.2 | NS |
| Nodules | 10/55 | 47/267 |  
| Vasculitis | 3/55 | 3/267 | 0.06 |
| Ritchie's score | 8.1 ± 8 | 10.7 ± 7.7 | NS |
| Lee's score | 11.3 ± 7.3 | 12 ± 7.7 | NS |
| ESR | 43.6 ± 30.2 | 50.9 ± 34.8 | NS |
| CRP | 32.02 ± 33 | 50.5 ± 56 | 0.005 |
| Latex+ | 37/54 (69%) | 158/264 (70%) | NS |
| Antinuclear antibodies+ | 18/53 (34%) | 83/258 (32%) | NS |
| C4 | 24.8 ± 9.3 | 28 ± 10.2 | 0.037 |
| CH50 | 73.5 ± 16.7 | 76.75 ± 16.37 | NS |

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