Palindromic rheumatism. II. Failure to detect circulating immune complexes during acute episodes

B. THOMPSON, I. MOHAMMED*, E. J. HOLBOROW, AND H. L. F. CURREY
From the Bone and Joint Research Unit, The London Hospital Medical College, London

SUMMARY Thirty-eight samples of blood and 2 of synovial fluid were obtained from 19 patients suffering from palindromic rheumatism. In 12 cases samples were obtained from the same patient both during and between acute attacks. The presence of immune complexes was sought by a C1q-binding test. Most patients gave negative results: moderately elevated levels were obtained in a few. Broadly the pattern of results showed that individual patients were either positive or negative irrespective of whether they were in an attack or in remission. C3 and C4 measurements showed no significant abnormalities, confirming previous studies. Patients with elevated C1q-binding tests tended to be seropositive. We speculate that these are patients more likely to develop rheumatoid arthritis.

In a recent publication from this Unit (Wajed et al., 1977) we reported clinical studies which pointed to palindromic rheumatism being a variant of rheumatoid arthritis. Patients presenting in this manner either evolved into typical rheumatoid polyarthritis or remained palindromic, and we found no evidence to suggest that these 2 groups were suffering from different disorders. A number of clinical features of the palindromic attacks led us to speculate that they might represent activation of the complement system by circulating immune complexes. We therefore studied serum complement levels in the same patients both during and between acute attacks. The results provided no evidence of any depression of complement activity either during or between attacks.

Complement depression is an indirect indication of the presence of circulating immune complexes, and for this reason we have reviewed again our patients with palindromic rheumatism, including some cases not reported in the previous publication, and tested their serum for the presence of immune complexes by a C1q-binding test. C3 and C4 complement components were also measured.

Materials and methods

Patients
Hospital notes of patients indexed as suffering from palindromic rheumatism were checked, and those who appeared still to be palindromic were asked to attend for review. Patients were questioned and examined, and the laboratory results were reviewed to establish whether they were still experiencing typical episodic attacks (Wajed et al., 1977) without evidence of having evolved into the picture of rheumatoid arthritis. Patients who satisfied these criteria were asked to provide samples of blood both during and between acute episodes.

Blood samples
Samples, in plain glass containers for serum and EDTA (sequestrene) bottles of plasma, were separated within 2 hours and stored at −20°C until tested. Each sample was thawed only once.

Immune complexes and complement measurements
C1q-binding activity was measured by the method of Zubler et al. (1976) as modified by Casali et al. (1977). This includes the use of Tween 20 to reduce background binding. The mean binding for 147 normal subjects was 6 ± 2%. Values above 10% are considered raised.

Plasma C3 and C4 were measured by radial immunodiffusion (Mancini et al., 1966). The normal ranges are: C3, 63–145 mg/dl; C4, 20–45 mg/dl.
Results

Thirty-eight samples of blood and 2 of synovial fluid were obtained from 19 patients. In 12 cases samples were obtained from the same patient both during and between acute attacks. The results of the Clq-binding and complement tests are set out in Table 1.

Most patients had normal Clq-binding levels both during and between attacks. Two (cases 5 and 17) had moderately elevated levels both during an attack and while in remission. Two patients (cases 2 and 10) had elevated values only during an attack, with normal interval values. Case 13 had elevated values for 2 samples obtained during remission, but we failed to get a specimen during an attack. Case 3 had a normal Clq-binding value both while in remission and also at the height of an extremely acute attack affecting a knee. Synovial fluid from this knee taken at the same time also gave a normal value. Synovial fluid obtained from a less acutely inflamed knee joint (case 11) showed a slightly raised Clq-binding level. C3 and C4 levels were measured on most of the blood samples but as before showed no significant departure from normal. However, comparison of the Clq-binding levels and the results of latex tests for rheumatoid factor show clearly that patients with elevated Clq-binding levels are more likely to be seropositive.

Discussion

If our assumption is correct that palindromic rheumatism is a variant of rheumatoid arthritis, then it is a condition of particular interest from the point of view of pathogenesis and possibly of aetiology. Unlike fully developed rheumatoid arthritis it offers the opportunity to study the same patient both during acute episodes and between attacks.

We have exploited this to test the hypothesis that the acute episodes result from the presence of circulating immune complexes. Our complement studies have shown no evidence of decreased levels during acute attacks. Clq-binding activity is regarded as an index of the presence of immune complexes, and measurements by this technique broadly agree with the results of immune complex identification by more direct methods.

Our results do not provide support for the hypothesis that palindromic attacks are due to the appearance of immune complexes in the circulation. Generally our patients gave either positive or negative results in the Clq-binding test irrespective of whether the patient was in an attack or in remission. It is nevertheless of considerable interest that patients with elevated Clq-binding levels (whether in an attack or in remission) were also those more likely to have positive tests for rheumatoid factor.

More than 80% of seropositive rheumatoid arthritis patients have raised blood levels of Clq-binding (Thompson and Holborow, unpublished), and the present findings, together with previous clinical experience (Wajed et al., 1977), suggest that, among patients with palindromic rheumatism, those with elevated Clq-binding tests are more likely to develop typical rheumatoid arthritis.

References

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B Thompson, I Mohammed, E J Holborow and H L Currey

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