

# Case Report: Rhupus (The Association of Systemic Lupus Erythematosus and Rheumatoid Arthritis): About 2 Cases

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## Abstract

**Introduction:** The association of systemic lupus erythematosus and rheumatoid arthritis (rhupus) is a rare clinical condition. Throughout the world, 287 cases of Rhupus have been described. We report two new observations of two patients who presented predominantly distal erosive polyarthrititis with positive anti-Sm antibodies in one case and SmRNP in the other case. **Observations:** Case 1: 37 years old patient, with a recent diagnosis of pulmonary tuberculosis. She has since 8 months an inflammatory, bilaterally and symmetrical polyarthralgia without deformation or ankylosing synovitis, associated with malar erythema without other abnormalities. Immunological tests showed: positive Rheumatoid factor at 158 IU/ml, positive Anti-CCP at 550 IU/ml, and positivity of antinuclear at 1/1280 nuclear fluorescence with a strong presence of anti-Sm >8 IU/ml. The diagnosis of rhupus was concluded, without serious visceral involvement. Case 2: A 28-year-old patient, married with 3 children, with bilateral, symmetrical, deforming and chronic polyarthrititis affecting large and small joints, which had been evolving for over 5 years without cutaneous abnormality associated. Paraclinical investigations showed: a biological inflammatory syndrome. Immunology was positive, with rheumatoid factors at 78 IU/ml, anti-CCP at 561 IU/ml, antinuclear antibodies at 1/1280 with positive anti-SmRNP and anti-SSA/Ro52, and a positive direct Coombs test. Joint ultrasound revealed tenosynovitis of the extensors and common flexors of the fingers, erosions and synovitis of multiple PPIs. The diagnosis of rhupus was based on the presence of 10 ACR criteria for RA and 8 ACR/EULAR 2019 criteria for SLE. **Conclusion:** Rheumatoid arthritis is a rare autoimmune disease combining features of both systemic lupus erythematosus and rheumatoid arthritis in the same patient, often sequentially. Despite a growing number of case reports and series, a consensus on the clas-

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sification of SLE arthritis is still lacking, and diagnostic criteria for rhupus do not exist. These cases of rhupus must be recognized, as the vital and/or functional prognosis may be different from SLE alone or isolated RA.

## Keywords

Rhumatoïd Arthritis, Lupus, Rhupus, Connective Tissue Disease

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## 1. Introduction

The coexistence of two or more connectivities in the same patient is a rare phenomenon, particularly the coexistence of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). It was first described by Shur in 1971 under the term Rhupus [1]. Toone [2] reported the first clinical observation in 1960 for better identification of this entity. Worldwide, 287 cases of rhupus have been described [3]. The most comprehensive and restrictive definition reported is compliance with the SLICC 2012 ACR criteria for SLE and ACR/EULAR 2010 for RA, associated with the presence of joint erosions, organ damage typical of SLE, FR antibodies or anti-CCP, ANA, native DNA or anti-Sm antibodies [3].

We report two new cases.

## 2. Observations

### Observation 1:

A 33-year-old female patient consulted for an altered general condition. She is unemployed, divorced, without child, and she doesn't use tobacco and alcohol. She had pulmonary bacilliferous tuberculosis diagnosed 3 months ago, for which she is on the current national combined anti-tuberculosis treatment.

Her clinical history began 8 months ago with inflammatory, bilaterally and symmetrical polyarthralgia without deformation or ankylosing synovitis, associated with malar erythema without other abnormalities. Immunological tests showed: positive Rheumatoid factor at 158 IU/ml, positive Anti-CCP at 550 IU/ml, and positivity of antinuclear at 1/1280 nuclear fluorescence with a strong presence of anti-Sm >8 IU/ml. The diagnosis of rhupus was concluded, by the ACR criteria for RA and ACR/EULAR for lupus. The complete check-up didn't find any serious visceral involvement.

### Observation 2:

A 28-year-old patient, married with 3 children, came to our clinic. She had secondary amenorrhea lasting 2 years, and was suffering from micropolycystic ovarian dystrophy treated with dydrogesterone. On admission, she presented with bilateral chronic polyarthritis affecting large and small joints, which had been evolving for over 5 years. The Questioning revealed a history of weight loss and hair loss, but no xerostomia or xerophthalmia. The physical examination revealed an apyretic patient in good general condition, with non-scarring alope-

cia and no other skin manifestations, bilateral symmetrical polyarthritis affecting the large (shoulders and elbows) and small joints, with synovitis of all the proximal interphalangeal and bilateral involvement without synovitis of the 2nd, 3rd and 5th metacarpophalangeal joints 2, 4 and 5, mallet deformity of the 5th proximal interphalangeal and reducible buttonhole deformity of the 3rd proximal interphalangeal. Paraclinical investigations showed: a biological inflammatory syndrom with a positive CRP 76 mg/l and a SV 110 mm at the first hour. Immunology was positive, with rheumatoid factors at 78 IU/ml, anti-CCP at 561 IU/ml, antinuclear antibodies at 1/1280 with positive anti-SmRNP and anti-SSA/Ro52, and a positive direct Coombs test. Joint ultrasound revealed tenosynovitis of the extensors and common flexors of the fingers, erosions and synovitis of multiple PPIs. The diagnosis of rhupus was based on the presence of 10 ACR criteria for RA and 8 ACR/EULAR 2019 criteria for SLE.

### 3. Discussion

In 1936, Friedberg *et al.* [4] first pointed out that SLE could mimic RA, with involvement of both large and small joints. In 1950, arthritis was proposed as a diagnostic feature of SLE by Daugherty *et al.* [5]. In 1960, Toone *et al.* were the first to report the coexistence of SLE and RA in 15 patients. The term “rhupus syndrome” was first used by Shur in 1971 [3].

The most comprehensive and restrictive definition reported is compliance with the SLICC 2012 ACR criteria for SLE and ACR/EULAR 2010 for RA, associated with the presence of joint erosions, organ damage typical of SLE, FR antibodies or anti-CCP, ANA, native DNA or anti-Sm antibodies.

The highest prevalence of rhupus (9.7%) was found in a prospective cohort of 103 lupus patients who all underwent systematic screening for erosions by ultrasound or MRI of the hands and wrists [6]. Its etiopathogenesis is a subject of controversy and includes genetic factors with a high frequency of HLA DR1/HLA RD2 alleles, hormonal factors especially sex hormones and environmental factors [7].

All our two observations of rhupus are reported in women, in whom 9 out of 10 cases of lupus and RA are diagnosed. In Sub-Saharan Africa and elsewhere, the predominance of women in systemic autoimmune diseases is classic [8]. It is highlighted by Anhouandogbo, who had a sex ratio of 0.219 [9], and by Kane [10] in their connectivitis cohort. In their systematic review of Rhupus, Antonini *et al.* noted a female predominance ranging from 84% to 100%. This is partly attributable to the role of sex hormones in modulating immune responses, and to certain defects in X chromosome inactivation.

In both our patients, the discovery of lupus disease and RA were concomitant. Even if the time to consultation is long, due to the similarity of joint symptoms in cases where there is very little synovitis and no deformity, it is difficult to describe the chronology of onset of these two pathologies. Nevertheless, it is interesting to note that rhupus is a sequential disease in which the features of RA and

SLE are rarely diagnosed simultaneously. Very often, RA is diagnosed first in 2/3 of patients, while the remainder are diagnosed either with SLE first (most often) or directly with rhus [3]. Thus, the classic symptoms of RA predominate and precede those of SLE in time, particularly rheumatoid nodules, which are frequent in this particular case and are seen in 40% of cases [3] [11]. This latter feature was not found in any of our patients. Nevertheless, in one of our patients, a hematological disorder of the autoimmune hemolytic anemia type is at the forefront of the picture, associated with classic cutaneous and articular involvement. This condition is often associated with rhus, but usually manifests as leukopenia and thrombocytopenia. It is often associated with mucocutaneous involvement (malar rash, photosensitivity and alopecia) and serous involvement (pleural and pericardial effusion). CRP, which is often negative or only slightly elevated in lupus, tends to be positive in rhus, sometimes at very high levels, as in our patients [3] [11].

Our patients also showed a marked increase in rheumatoid factors (10.53 and 5.2 times normal, respectively) and anti-CCP (27.5 and 28.05 times normal, respectively). Indeed, it has been described that the prevalence of these markers is significantly higher than in SLE patients, with no difference or decrease in values found compared to RA patients [3] [6] [7]. In particular, in one study, rhus patients had a 23-fold higher concentration of anti-CCP antibodies than SLE patients [11]. The positive and negative predictive values of anti-CCP antibodies for rhus were 0.62 and 0.91 respectively in a cohort of 377 lupus patients [3]. Furthermore, compared with SLE patients, rhus patients have a higher prevalence of positive antinuclear, anti-dsDNA and anti-Sm antibodies, whereas RA patients have a lower prevalence of anti-dsDNA antibodies [3] [6] [11]. As regards anti-phospholipid antibodies (APL), anti-ribonucleoprotein antibodies (RNP) and other ENA, no difference in prevalence has been found between rhus and SLE patients in some studies [3] [6]. Others, however, report a high frequency of anticardiolipin antibodies, albeit with what appears to be a low thromboembolic risk [11]. As for the frequency of hypocomplementemia, it was sometimes lower [6] in patients with rhus and sometimes higher [11], and therefore varied from study to study. Thus, in rhus, lupus-like extra-articular involvement tends to be less frequent and less severe than in SLE. Nevertheless, these cases of rhus must be recognized, as the vital and/or functional prognosis may be different from SLE alone or isolated RA [12] [13].

#### 4. Conclusion

Rheumatoid arthritis is a rare autoimmune disease combining features of both systemic lupus erythematosus and rheumatoid arthritis in the same patient, often sequentially. Joint involvement is constant and similar to that of RA, while lupus-like extra-articular involvement tends to be less frequent and less severe than that of SLE. Despite a growing number of case reports and series, a consensus on the classification of SLE arthritis is still lacking, and diagnostic criteria for rhus do not exist. Large prospective studies evaluating patients from first

symptoms through a long follow-up period are needed to better understand this sequential and dynamic overlapping disease and characterize its clinical and immunological phenotype.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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