

# Rhupus: Illustration about four Senegalese Cases

Ndao A.C.<sup>1</sup>, Diallo R<sup>2</sup>, Diagne N.<sup>3</sup>, Kane B.S.<sup>4</sup>, Djiba B.<sup>5</sup>, Dieng M.<sup>6</sup>, Faye A.<sup>7</sup>, Ndongo S.<sup>8</sup>, Diallo S.<sup>9</sup>, Pouye A.<sup>10</sup>

<sup>1, 2, 3, 4, 5, 6, 7, 8, 10</sup>Department of Internal Medicine

<sup>9</sup>Department of Rheumatology

**Abstract:** ***Introduction:** Rhupus is a combination of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). It is a rare entity whose existence is often controversial. Since its first description in 1971 by Schur, fewer than 150 cases have been described in the literature. We are reporting four observations. **Materials and methods:** A retrospective study, carried out between August 2011 and March 2014 in the Department of Internal Medicine at the University Hospital Aristide Le Dantec, was used to collect the observations of patients with rhupus. The diagnosis of RA and SLE was based on epidemiological, clinical and paraclinical arguments in accordance with the ACR / EULAR 2010 criteria for PR and ACR 1997 for SLE. **Observations:** Four observations were collected in 2 women and 2 men of average age 33 years (extremes: 28 years and 36 years). They all had chronic polyarthritis (1 to 10 years of evolution), polysynovial, and peripheral with irreducible deformations in 3 patients with ulnar stroke type, ankylosis of the wrists and buttonhole. The extra-articular manifestations were rheumatoid nodules (1 case) and an erythema malar in vespertilio and decollete (1 case). A non-specific biological inflammatory syndrome was present in all patients. Two patients had lymphopenia at 1176 and 1220 / mm<sup>3</sup>. On the immunological level, there was a positivity of rheumatoid factors (1 case), anti-nuclear (1 case with speckled fluorescence), anti-CCP antibodies (3 cases), anti-RNP antibodies (3 cases) Anti-SmRNP (3 cases), and anti-Sm (3 cases), anti-SSA / Ro and SSB / La (1 case). The standard X-ray showed a demineralization of the bones of the carpus and epiphyseal in bands (1 case), a radio carpal pinching (2 cases) and proximal interphalangeal (2 cases), a carpite (3 cases), an erosion of the head of proximal phalanges and metacarpals (3 cases). Radiography of the hands and feet was normal in one patient. A therapeutic management combined low-dose of corticosteroids (4 cases), hydroxychloroquine (4 cases) and methotrexate (3 cases). The progression was favorable in 2 patients, one had persistent monoarthritis moderately responding to infiltration and one patient was lost from view. **Conclusion:** Although rarely reported in the literature, the association of rheumatoid arthritis and lupus remains a reality. Thus, in the face of any systemic pathology, attention must be paid to the other associated autoimmune diseases.*

**Keywords:** rheumatoid arthritis, lupus, rhupus, anti-CCP, anti-Sm

## 1. Introduction

The coexistence of two or more systemic diseases in the same patient is possible but infrequent. The association of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) called rhupus, the existence of which remains controversial, is all the more rare. Its prevalence is estimated at 0.09% [1]. Since the first observation reported by Toone in 1960 [2] and its first description in 1971 by PH Schur [3], fewer than 150 cases have been described in the literature. We are reporting four observations.

## 2. Observations

**Observation 1:** This is a 33-year-old patient received in consultation in August 2011, in the internal medicine department of the Aristide Le Dantec Hospital of Dakar University Hospital, for peripheral chronic joint pain, evolving over the past 10 years, interesting the metacarpal-phalangeal (MCP), proximal interphalangeal (IPP), metacarpal-phalangeal (MTP), wrists, ankles, elbows, shoulders, knees with involvement of the cervical spine. This arthritis was bilateral, symmetrical, evolving by thrust and remission.

She was attended the department of dermatology, from the same hospital, from 1997 to 1998, for a lupus disease. She had been put on prednisone and hydroxychloroquine and then she discontinued this treatment without medical advice after a year.

Physical examination had shown the presence of synovitis at the ankles and PPIs of the hands, a skeletal test positive for MCP, deformities of the type of bilateral ulnar stroke and buttonhole at the 3rd radius. The extra-articular signs were made of erythema malar in vespertilio and erythema at the decollete (anterior face of the thorax).

Biology revealed a non-specific biological inflammatory syndrome (SIBNS) with a rate of sedimentation (SV) at 50mm at the first hour, a C-reactive protein (CRP) at 32mg / L, anemia (hemoglobin = 9.4 g / dl) microcytic hypochrome. White blood cells were at 7 800 / mm<sup>3</sup> (neutrophils at 4 000 / mm<sup>3</sup>, lymphocytes at 4200 / mm<sup>3</sup>), the platelet count was 318 000 / mm<sup>3</sup>. The 24-hour proteinuria was 0.03 g. Transaminases, urea and serum creatinine were normal. The serology of viral hepatitis B and C was negative.

At immunology, Waaler Roses' reaction was positive at 36 IU / mL, anti-CCP antibodies were positive at 69 IU / mL (N < 5). However, anti-RNP, anti-Sm, anti-SSA and anti-SSB antibodies were negative. Native anti-DNA and anti-nuclear antibodies were not searched.

The X-ray of the faced hands showed a pinching of the joint spacing to the PPIs, the erosions and geodes to the 3rd PPI. Thus the diagnosis of rhupus was retained in front of this chronic, erosive, deforming polyarthritis associated with a positivity of the anti-CCP in a young woman. Treatment based on methotrexate, hydroxychloroquine and prednisone was instituted with a good evolution.

**Observation 2:** Patient of 36 years, followed in the same department since October 2012, for polysynovial, chronic, bilateral, symmetrical, peripheral, non-deforming polyarthritis reaching the PPI, MCP, wrist, ankle, shoulders and left knee without extra-articular signs and evolving for 1 year.

Biology had demonstrated an acceleration of SV at 30 mm, normal CRP at 3.1 mg / L, anemia at 10.6 g / dl, microcytic hypochromium. Leukocytes were at 4,200 / mm<sup>3</sup> and platelets at 338,000 / mm<sup>3</sup>. The 24-hour proteinuria was absent. Transaminases, serum creatinine were normal and the serology of viral hepatitis B was negative.

X-rays of the hands, feet and thorax were normal.

Immunological analyzes showed a positivity of anti-CCP antibodies at 148 IU / mL, anti-U1 RNP at 1.8 IU / mL, anti-Sm RNP greater than 8 IU / mL and anti-Sm at 3.1 IU / ML. Thus the diagnosis of rhus was made in front of the chronic polyarthritis, the normal CRP and the results of the immunology.

The evolution, under Methotrexate, folic acid, prednisone and hydroxychloroquine, was marked by the persistence of monoarthritis of the right wrist responding moderately to infiltration.

**Observation 3:** 28-year-old patient received in May 2013 for chronic, bilateral, symmetrical polyarthritis, evolving by spontaneous relapses and relapses, involving wrists, MCPs, IIPs (hands), PDI, IPDs, elbows, shoulders and knees. Physical examination noted deformities in the form of bilateral ulnar wobbling and extra-articular signs with rheumatoid nodules at the elbows. It had a SIBNS with an SV at 34 mm at the first hour, a CRP at 96 mg / L, an anemia at 8.2 g / dL normocytic hypochrome. Lymphopenia

at 1 176 / mm<sup>3</sup> was noted. Leukocytes, neutrophils, platelets, transaminases and the serum creatinine were normal. The serology of viral hepatitis B was negative.

The antibody assay showed a negativity of rheumatoid factors, anti-CCP, native anti-DNA and a positivity of U1 RNP greater than 8UI / mL, Sm RNP greater than 8UI / mL and Sm greater than 8UI / mL

The X-ray of the hands showed a demineralization in epiphyseal band and carps, a left wrist radiograph and IPP with head erosion of the right 5th IPP.

The diagnosis of rhus was retained based on erosive arthritis, rheumatoid nodules, lymphopenia, and high anti-Sm positivity.

He had been put on hydroxychloroquine and prednisone but the treatment could not be evaluated because he was loss of sight of. He was not on methotrexate for his fear of side effects on fertility.

**Observation 4:** This was a 35-year-old man, followed since March 2014 for chronic polyarthritis, peripheral to large and small joints with presence of synovitis, deforming to the left ulnar wing type, ankylosis of the wrists and buttonhole to the 3rd and 4th rays to the left. This table had evolved a year before its first consultation. The extra-articular signs consisted of lesions of vitiligo at the back level.

In the presence of chronic, peripheral, deforming, erosive polyarthritis, lymphopenia, the positivity of anti-CCP and anti-Sm; the diagnosis of rhus was retained. He was put on methotrexate, folic acid, hydroxychloroquine and prednisone with a favorable development.

**Table 1:** Clinical and paraclinical manifestations of the rum of the 4 patients

| Observation  | 1   | 2  | 3   | 4  |
|--|---|--|---|--|
| Sex  | Female  | Female   | Male  | Male   |
| Age  | 33 years  | 36 years   | 28 years  | 35 years   |
| Signs and joints   | Chronic polyarthritis (10 years) peripheral polysynovial erosive  | Non-deforming polysynovial peripheral chronic polyarthritis (1 year) | Chronic polyarthritis (4 years) peripheral polysynovial with hand of Jacoud                                     | Chronic polyarthritis (1 year) peripheral polysynovial erosive |
| Extra-articular signs  | - Erythema malar in vespertilio<br>-Decreased erythema            | Nil  | Rheumatoid nodules  | Back vitiligo lesions  |
| VS (mm/H1)   | 50  | 30   | 34  | Not done   |
| CRP (g/dl)   | 32  | 3,1  | 96  | Not done   |
| Hemoglobin   | Hb: 9.4 g / dl microcytic hypochrome                              | Hb: 10.6 g / dl microcytic hypochrome                                | - Hb: 8.2 g / dl hypochrome normocytic<br>- Lymphocytopenia at 1176/ mm <sup>3</sup>                            | Lymphopenia at 1220 / mm <sup>3</sup>                          |
| Rheumatoid Factors   | WR : 36UI/ml  | Not done   | Negative  | Not done   |
| Anti-CCP   | 69 UI/ml  | 148 UI/ml  | Negative  | 200 UI/ml  |
| ANA  | Not done  | Not done   | Not done  | 1/640, speckled appearance                                     |
| Anti-ECT (U1RNP, SmRNP, Sm, SSA / Ro, SSB / La, Jo1, Scl70, centromeres) |   | U1RNP > 8 UI/ml<br>SmRNP > 8 UI/ml<br>Sm : 3,1 UI/ml                 | U1RNP > 8 UI/ml<br>SmRNP > 8 UI/ml<br>Sm > 8 UI/ml  | U1RNP 3,2<br>Sm > 8<br>SSA/Ro 3<br>SSB/La 2,6                  |
| Anti-DNA   | Not done  | Note done  | Negative  | Not done   |
| Radiography of hands and feet  | Pinching of PPI interlining<br>Erosion and geodesy at the 3rd IPP | normal   | Demineralization of carp bones and epiphyseal band<br>- Carpal tunneling<br>- Head Erosion at the right 5th IPP | Bilateral carpite  |

### 3. Discussion

Rhupus is defined by the association of erosive deforming peritoneal arthritis of RA with clinical signs of SLE with the presence of autoantibodies specific for these two conditions (rheumatoid or anti-CCP factors for RA and anti-DNA or anti-Sm for the LES) [4]. It is a rare entity whose existence is often controversial.

Our series reports the presence of a rhupus in two women and two men. However, unlike our series, the clear female predominance of this syndrome has been reported in several publications [5, 6]

This could be explained by the small number of our series.

The average age of our patients was 33 years, which is consistent with the data found in the literature. Indeed, rhupus mainly concerns the young woman in the third decade [7, 8, 9]

This could be explained by the small number of our series.

In the majority of cases, the diagnosis of RA was made concurrently with the diagnosis of lupus. PR may precede lupus, car studies in the production of anti-nuclear antibodies in patients followed prolonged for RA [10].

Simon et al. [11] demonstrated that patients with rheumatoid arthritis had first manifestations of RA and then, on average, 4 years later, clinical signs and biological abnormalities appeared in favor of SLE.

In the study by Sparsa et al. [6], RA pre-dicted the diagnosis of lupus in ten cases; whereas in 6 patients the diagnosis of rhupus was concomitant. The predominant signs of RA were erosive arthritis and rheumatoid nodules, whereas LES manifestations were generally minor, such as photosensitivity, hematological abnormalities [12]. In the largest cohort on rhupus with 28 patients, only one had proliferative type III glomerulonephritis and two had proteinuria greater than 0.5 g / 24 h and no other visceral or haematological involvement was found [6]. However, more severe manifestations of SLE have been reported [13, 14].

The clinical manifestations of rhupus in our patients were mainly articular and cutaneous. Polyarthritis is one of the most frequent clinical manifestations of lupus [15, 16] and RA. However, it is classically non-erosive during SLE, whereas RA is characterized by the early onset of erosions [17]. Cases of deforming and erosive SLE were nevertheless reported in approximately 5% of patients followed for SLE [18, 19]. Only one patient presented clinical signs suggestive of lupus with malar erythema. Visceral involvement is rarely described [14].

In our series (Table I), only one patient showed no destructive lesions on the standard X-ray of the pathways and feet, knowing that she was seen in an evolution and that the articular ultrasound neither the dedicated MRI was realized on her in order to formally eliminate erosion. It has been reported that most patients with RA develop erosive arthritis after two or three years of development [17]

All other cases met the diagnostic criteria of rhupus and were consistent with the literatures' data.

On the paraclinic level, 3 of our patients showed immunological signs suggestive of lupus associated with RA with positive anti-CCP and anti-Sm (the latter being strongly suggestive of lupus).

The antibodies anti-peptides cyclic citrullinated (CCP) are classically considered as a diagnostic marker of high sensitivity and specificity in RA [20, 21]. However, recent work has shown that anti-CCPs can be detected in other conditions [22, 23] and in particular Sjögren's syndrome [24] and SLE [25, 26]. The presence of these antibodies in these diseases, especially in SLE, is a predictive serum marker for early and erosive polyarthritis [22, 26, 27]

### 4. Conclusion

Rhupus is a rare but real entity. To the question "rhupus myth or reality? ", A formal response will be difficult to make. Is it a SLE with a deforming erosive polyarthritis sometimes (Jaccoud's rheumatism) and anti-CCP positivity or actually a PR and SLE overlap syndrome? It can be considered as a real entity insofar as a high anti-CCP antibodies level greater than 50 IU / mL is specific for RA.

### 5. Conflicts of Interest

None

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