Case Report

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Rhupus syndrome. a case report of a rare combination

Tasneem Drie, MD[a,*], Naram Khalayli, MD[a], Ghina Haidar, MD[a], Diaa Haj Ali, MD[b]

Introduction and importance: Rhupus syndrome is a very rare combination of systemic lupus erythematosus and rheumatoid arthritis. It is characterized by the presence of erosive arthritis with symptoms and signs of systemic lupus erythematosus. Rheumatoid nodules and neurological and renal involvement are further complications of Rhupus syndrome, leading to a worse prognosis.

Case presentation: The authors presented a young female patient diagnosed with lupus erythematosus, who laterally, developed clinical signs and biomarkers that led to the diagnosis of Rhupus syndrome. This is believed to be of relevance to the knowledge of the medical community.

Conclusion: Despite being a rare entity, it is important to know its early diagnosis, and treatment to reduce the complications

Keywords: Autoimmunity, overlap, rheumatoid arthritis, rhupus syndrome, systemic lupus erythematosus

Introduction

Rheumatic diseases (RDs) include 250 conditions characterized clinically by arthritis, and decreased quality of life[1].

Although, specific criteria were found by different collegues, groups, and leagues to diagnose these RDs, up to 25% of patients cannot be diagnosed as they did not meet the criteria for a specific disease[2].

Multiple overlap syndromes between two or more RD are found and considered as an independent entity, as is the case of mixed connective tissue disease[3].

The coexistence of SLE and RA was first reported in 1960 while the term Rhupus syndrome (RhS) was first coined by Peter Schur in 1971. Rhupus syndrome is a rare, neglected autoimmune entity with features of both RA and SLE that mostly appear sequentially[4], with an estimation between 0.01% and 2% of patients[3].

RhS is defined as a deforming and erosive symmetric polyarthritis accompanied by symptoms and signs of SLE and the presence of antibodies of high diagnostic specificity, such as anti-double stranded DNA, anti-Smith and anti-cyclic citrullinated peptide (anti-CCP)[3,4].

HIGHLIGHTS

- Rhupus syndrome is a very rare combination of systemic lupus erythematosus and rheumatoid arthritis.
- Despite being a rare entity, it is important to know its early diagnosis, and treatment to reduce the complications
- Most of the published cases described the typical course of the syndrome as the onset of manifestations of rheumatoid disease followed by manifestations of lupus, but in our case, we describe a case of a woman who was diagnosed with lupus first and then after 6 years developed articular manifestations given by chronic, symmetric, seropositive polyarthritis.

We decided to publish this case report to let the medical community know more about RhS as it is infrequent.

Our study is compatible with the SCARE Guideline checklist[5].

This case is submitted on the research registry dashboard[6]

Case presentation

A 22-year-old female patient, married, non-smoker, with a diagnosis of SLE for 3 years, according to ACR/EULAR2019 criteria(5), as she met the following diagnostic points fatigue, low-grade fever, malar rash, oral ulcers, photosensitivity, alopecia, arthralgia, positive antinuclear antibodies (ANAs) at1/160, and leukopenia.

Current treatment includes 5 mg of prednisone daily, and 200 mg/day of hydroxychloroquine. She had no comorbidities or positive family history.

During the 6 years of evolution of the disease, she presented periods of exacerbation with a predominance of joint manifestations and constitutional symptoms that resolved with the

[a]Faculty of Medicine, Damascus University, Damascus and [b]Syrian Private University, Daraa, Syria

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*Corresponding author. Address: Damascus University Faculty of Medicine, Damascus, Syrian Arab Republic. Tel.: +963 948 958 318.
E-mail: samsomadrei@gmail.com (T. Drie).

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increase in the dose of steroids up to 35 mg(1/2 mg/Kg/day), and hydroxychloroquine up to 400 mg/day. She was followed up every 3–6 months.

On her last visit, she presented complaining of fatigue, loss of appetite, and low-grade fever, in addition to additive inflammatory joint pain in the small joints of the hands and feet, as well as the shoulders, the elbows, and the knees, accompanied by morning stiffness lasting 2 h.

Physical examination revealed fever less than 38.5*, arthritis of hands and feet, as well as the shoulders, the elbows, and the knees, oral ulcer, and a slight malar rash(Fig. 1). Inflammatory signs of arthritis are given by pain spontaneous and induced by mobilization, heat, and an increase in volume. Atrophy of the interosseous muscles of both hands, bilateral swelling of the second, third, and fourth metacarpophalangeal joints, and the proximal interphalangeal joints were seen (Fig. 2).

Laboratory tests revealed: white blood cells 3200/mm^3 ($n = 4000–11\ 000$)/mm^3, erythrocyte sedimentation rate = 62 mm/h^1 ($n = 0–20$), C-reactive protein at128 mg/dl ($n < 6$), haemoglobin = 9.3 g/l (n:12–14) platelets = 195 ($n = 150–450$) The rest of the chemical tests were normal.

Immune profile showed positivity of ANAs > 1/160 U/mL, Anti-Smith 13 U/ml (0–7), Anti CCP (92 U/ml(20), rheumatoid factor 345 IU/mL(20 IU\ml). complements value was normal.

The Hands X-ray revealed osteopenia (Image 1)

The diagnosis of RhS was done according to the clinical presentation described above and the immunological tests and imaging studies.

We decided to increase the dose of steroid to 30 mg daily, and the treatment of by10 mg/week of methotrexate was initiated, with 5 mg/week of folic acid. 3 months later, the patient has evolved favourably remission clinically and laboratory.

Discussion

RhS is a rare condition consists of SLE and RA, that has its own clinical manifestations and laboratory markers, with female predominance[4].

There is a role of the immune system that has been confirmed by the presence of antibodies and immune complexes in serum profile. A glance through the previous case series has revealed the possibility of anti-CCP and C-RP as markers for the diagnosis of rhupus[3–7].

RA manifestations presented first, then those of SLE, in most cases. Conversely, reports of concurrent symptoms and vice versa are infrequent[7]. In our case, our female patient had a diagnosis of SLE for 6 years and then began having articular manifestations given by chronic, symmetric, seropositive polyarthritis, and for this reason, it differs from the generality of cases of RhS previously reported.

RA is a progressive chronic systemic inflammatory immune disease with articular and systemic effects. Its exact cause is unknown, but genetic and environmental factors are contributory[3].

In RA patients, the time for the onset of the clinical manifestations of SLE ranges between 4 and 7 years[3,7], while, in the case of SLE patients with initial SLE, is approximately 4 years for the onset of the articular manifestations of RA[2,3,8]. In our case study, this period was shorter since articular manifestations started 3 years after SLE diagnosis.

Rhupus patients have been found to have a lower incidence of malar rash, haemolytic anaemia, and renal and neurological

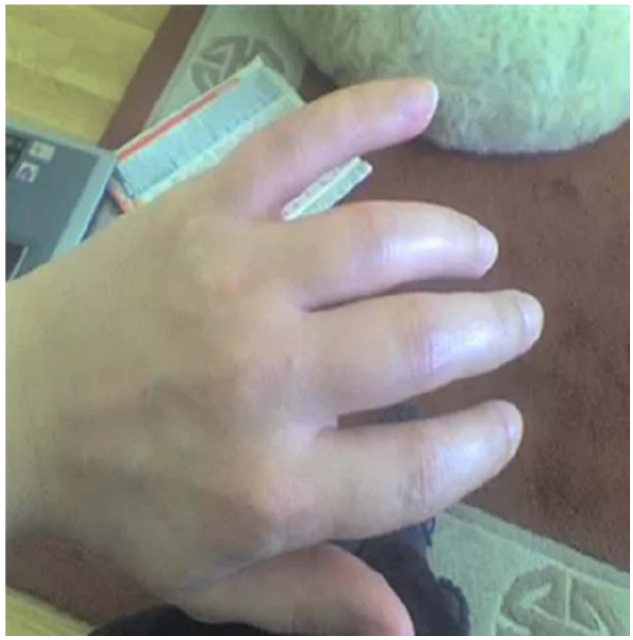

Figure 2. Swelling of metacarpophalangeal and proximal interphalangeal joints.

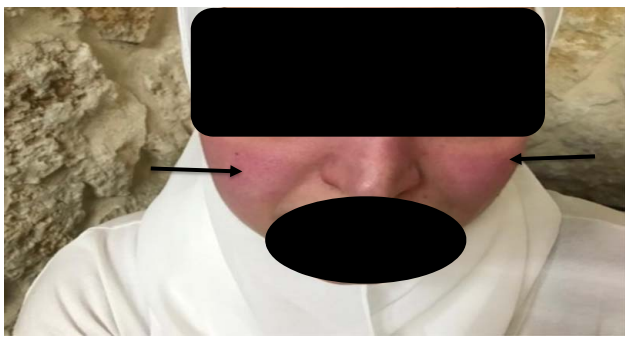

Figure 1. Malar rash.

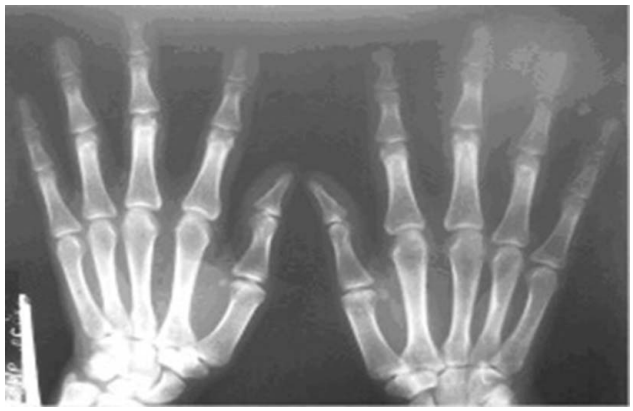

Image 1. Osteopenia.

involvement compared with the SLE group[8–10], as in our case. In addition, rhupus patients rarely have severe renal disorders such as nephrotic syndrome and renal insufficiency. The disease activity in SLE, initial corticosteroid dosages, or pulse have been found to be lower in the rhupus patients[3,7]. Previous studies have also shown that rhupus patients have a lower incidence of visceral organ involvement compared with SLE patients without RA[3]. SLE shows 3 types of articular involvement: intermittent non-erosive polyarthritis usually found in the hands, wrists, and knees; non-erosive deforming arthritis referred to as Jaccoud's joint; and arthritis with joint deformities and specific erosion, i.e., Rhupus syndrome. Most patients with SLE have transient, migratory, and reversible arthritis without erosion[3,8].

Some rheumatologists suggest that the presence of rheumatoid nodules in SLE patients could be a risk factor for Rhupus syndrome[3,10].

The definitive diagnosis of RhS is done according to the presence of specific immune markers such as anti-Smith or anti-CCP. In addition to the positivity of ANAs, and rheumatoid factor[3–10]. The presence of anti-CCP has been used to distinguish RA and Rhupus syndrome from SLE[10]. In our case, the positivity of anti-Smith and anti-CCP antibodies supports the criterion that Rhupus syndrome is an overlap syndrome and not a variable of SLE.

Hands X-ray may show juxta-articular bone demineralization and erosions which are part of the diagnostic criteria for RA[6,11].

Hydroxychloroquine, corticosteroids, and methotrexate are used to control the inflammatory arthritis and alleviate constitutional symptoms[3–10], as we did. Other treatments such as mycophenolate mofetil and biological therapy have been used in the presence of important organ involvement[3–10].

The neurological and haematological involvement lowered the quality of life[11]. Our patient had no renal or neurological involvement. The leukopenia responded well to the treatment.

This case of Rhupus syndrome presented in a 22 years old young female with mucocutaneous involvement, and erosive arthritis, with a good response to treatment with methotrexate.

The other 2 reported cases are different from ours:Urbano Solis Cartas and colleagues revealed a case of RhS in a 47-year-old female patient with a diagnosis of SLE for 6 years, presented with, mucocutaneous involvement, complement consumption, thrombocytopenia erosive arthritis with deformities. She had increased the dose of steroid to 15 mg daily and added 10 mg of methotrexate weekly[3]. Upadhyaya and colleagues revealed a case of RhS in a young unmarried female presented with high-grade fever spikes, mucocutaneous involvement, bilateral pleural effusion , and erosive arthritis, along with positive anti-ds DNA antibody, and low complement level (C3, C4). She was prescribed corticosteroids, hydroxychloroquine, and methotrexate. RhS was diagnosed within 6 months of SLE diagnosis[11].

Conclusion

Rhupus syndrome is a special overlap syndrome of RA and SLE that is characterized by more RA and less SLE-associated damage.The treatment and prognosis of Rhupus syndrome have been found to be different from that of RA or SLE. Thus, its early diagnosis is important for choosing suitable therapies, reducing the complications and improving patient prognosis, despite being a rare entity

Ethical approval

This case was approved by the Ethical Committee of the Faculty of Medicine, Damascus University.

Informed consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contributions

All authors described the case and collected the clinical data. reviewed and edited the manuscript.

Conflicts of interest disclosure

The authors declare that there are no conflicts of interest.

Research registration unique identifying number (UIN)

1. Name of the registry: Tasneem Drie.
2. Unique Identifying number or registration ID: research registry 9427.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-theregistry# home/.

Guarantor

Tasneem Drie, samsomadrei@gmail.com.

Data availability

Available.

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