Rhupus Case Series

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ABSTRACT

Presenting the three patients with rhupus with the predominance of symmetrical polyarthritis by ACR criteria for SLE as well as for RA, ANA positive all patients, and positive anti-DNA anti-CCP or rheumatoid factor positivity in high titers in all patients, positive anti-SSA in one patient, and positive anti-anti-Sm in one patient. Renal and liver function tests were normal in all patients. All patients responded well by DMRDs.

1. Introduction :

Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are autoimmune diseases with different clinical and serological features affecting various organs and systems. Although SLE can affect the skin, lungs, and kidneys, it can affect the joints in (90%). Rheumatoid arthritis has a worldwide prevalence of approximately in 0.5–1.0% of adult population and SLE prevalent in 6.5–27.7/100,000. "Rhupus" is a term used to describe patients with coexistence of RA and SLE . It is discussed that the question of whether RA and SLE occur in the same patient, the so-called "rhupus," or whether any deforming and erosive disease might be integral to the arthritis of SLE. There is evidence to support the presence of rhupus as a true overlap syndrome. Rhupus syndrome is a rare clinical entity which has an estimated prevalence rate of 0.09%.

2. Case Reports

2.1. Patient-1

A 50-year-old female was admitted with the complaints of intermittent pain in hand joints and morning stiffness for the past three years. She also have a history of fever, easy fatigability and recurrent oral ulcers for the last three years. On physical examination, she had oral cold sores, and her DAS-28 score was 20 with swan neck deformity on second and third finger of the right hand.

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Laboratory studies showed normal blood count, an erythrocyte sedimentation rate of 45 □ mm/h, C-reactive protein of 3.39 □ mg/dL which was negative, rheumatoid factor of 3.9 IU/mL, anti-CCP level of > 192.5 □ U/mL (strong positive), antinuclear antibodies (ANA) 1/100 positive speckled pattern, anti-dsDNA positive with 43.2 positive. Urinalysis was normal Urine protein-to-creatinine ratio (UP/CR) is 50 □ mg protein per gram creatinine (normal □ < □ 30 □ mg protein for 24 hours in urine). Renal and liver function tests were normal.

2.2. Patient-2

A 26-year-old female attended OPD with the complaint of pain in small joints of both hands for the last eighteen months. She gave a history of alopecia, Raynaud phenomenon, and oral ulcers. On physical examination, she had bilateral proximal interphalangeal joint tenderness, right knee joint swelling, and right wrist joint tenderness.

Laboratory studies showed normal blood count, an erythrocyte sedimentation rate of 54 mm/h, C-reactive protein of 12.40 mg/dL, rheumatoid factor of 84.2 IU/mL, anti-CCP level of 40 U/mL, ANA 1/100 speckled and homogenous pattern , anti-dsDNA negative, and anti-Sm positive. Urinalysis showed microscopic hematuria (red blood cells 6/high power field). Urine protein-to-creatinine ratio (UP/CR) is 35 mg. Renal and liver function tests were normal.

2.3. Patient-3

A 40-year-old female presented with the complaint of intermittent joint pain with morning stiffness for past four years. For the past 2 years, she also had oral

ulcers dryness of mouth and malar rash. On physical examination, she had right 4 proximal interphalangeal joint swelling and tenderness, left metacarpophalangeal tenderness, bilateral wrist joint tenderness, malar rash, oral ulcers, and morning stiffness.

Laboratory tests revealed a normal blood count, an erythrocyte sedimentation rate of 56?mm/h, C-reactive protein of 2.36 mg/dL, rheumatoid factor of 84.1 IU/mL, and anti-CCP level of 63.2 U/mL. The ANA was negative, anti-dsDNA, and anti-SSA were positive, but anti-Sm was negative. Urinalysis showed microscopic hematuria (red blood cells 7 / high-power field). Urine protein-to-creatinine ratio (UP/CR) is 40 mg protein per gram creatinine (normal < 30 mg protein / 24 hours in urine). Renal and liver function tests were normal.

3. Diagnosis and Treatment

Rhupus syndrome was diagnosed in three patients, and an oral treatment with methotrexate (15 mg / week), folic acid (5 mg / week), and hydroxychloroquine (200 mg / twice a day) were begun. Patients well responded by treatment and went for remission after 2-3 months.

4. Discussion

The term "Rhupus syndrome" is used to describe the coexistence of SLE and RA, wherein patients have symmetrical erosive arthritis and characteristic manifestations of SLE. The definition of Rhupus syndrome remains controversial, as the immunopathological process of SLE is considered to be the exact opposite of RA. Abnormal activation of T helper type 2 cell (Th2) cytokines plays a central role in SLE while T helper type 1 cells (Th1) participate in RA. Thus, the overlap of SLE and RA has a very low incidence (0.01%–0.2%) in patients with arthritis, and the incidence is < 2% in patients with connective tissue diseases. Mostly Rhupus syndrome patients were diagnosed with onset of RA (83.9%), some with onset of SLE, and the rest were diagnosed with SLE and RA concurrently. Arthralgia and arthritis are the most common symptom of SLE, and they occur very early in the disease course. About 90% of patients diagnosed with SLE have arthralgia or arthritis during their course and 34% of patients have arthritis at disease onset. Some rheumatologists have classified Rhupus syndrome as a subset of SLE with severe arthritis. SLE shows three types of articular involvement : intermittent nonerosive polyarthritis usually found in the hands, wrists, and knees; nonerosive deforming arthritis referred to as Jaccoud's joint; and arthritis with joint deformities and specific erosion, that is, Rhupus syndrome. Most patients with SLE have transient, migratory, and reversible arthritis without erosion. A few SLE patients have severe deformities in hands or feet, which was termed as Jaccoud's arthropathy with subluxation seen in plain radiolographs. Jaccoud's joint usually involves tendinitis, but not erosion, synovitis, or outstanding joint swelling or tenderness. Rhupus patients have lower incidences of malar rash, hemolytic anemia, and renal and neurological involvement compared with the control group. Rhupus patients rarely have severe renal disorders such as nephrotic syndrome and renal insufficiency. Whether Rhupus is a distinct entity with overlapping RA and SLE or is a subset of SLE is a subject of debate, as some patients with Rhupus have specific antibodies of SLE. In the present study, we demonstrated that Rhupus patients showed a prevalence of anti-double-stranded DNA and anti-Sm antibodies SSA that was similar to those of lupus patients without RA coexistence. However, Rhupus patients display a clinical and serological profile that differs significantly from SLE with more "robust" features of RA such as severe, erosive, and deforming arthropathy as well as a significantly high prevalence of RF and anti-CCP antibodies, while having mild SLE disease activity and much lower rates of visceral organ involvement . Our findings support the contention that Rhupus is an overlap of RA and SLE and not merely a specific subset of SLE.

The serum CRP level is usually normal or slightly increased in most patients with active SLE, and a highly elevated CRP level is almost always associated with infections. The anti-CCP antibody has high sensitivity and specificity for the diagnosis of RA and is significantly associated with

radiological joint erosion 18. Since RF and anti-CCP antibody positivity is associated with erosive arthritis, SLE patients with such indicators should be aggressively treated to control joint inflammation.

Very few data are available concerning Rhupus syndrome treatment, and the data that do exist are based on a few case studies and small series. Generally, treatment regimens including low-to-moderate dosages of corticosteroids with multiple DMARDs (e.g., methotrexate and leflunomide) could be used in Rhupus patients with prominent joint involvement to prevent the progression of erosive arthritis. Both mycophenolate mofetil and cyclosporin A were reported to be effective in treating Rhupus syndrome while tumor necrosis factor inhibitors showed little effect on Rhupus or SLE, and may even lead to disease aggravation, despite reports of their success in RA treatments, while rituximab and abatacept appear to be more promising in Rhupus treatments.

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