Editorial

Overlap syndromes: Rhupus

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An overlap syndrome is one that satisfies the classification criteria of at least two connective tissue diseases occurring at the same time or at different times in the same patient[1].

Any combination of existing rheumatic diseases has been reported, for example Systemic Lupus Erythematosus (SLE) and polymyositis, scleroderma and dermatomyositis, Rheumatoid Arthritis (RA) and scleroderma, rheumatoid arthritis and systemic lupus.

In this time, we revisit the controversial rheumatoid arthritis and SLE overlap syndrome also termed as 'Rhupus', first used by Schur in 1971[2]. While Schur coined the term, Toone *et al*[3] offered the first description of the disease.

Several definitions of rhupus have been offered. It has been defined as a condition in which patients present with a clinical picture of SLE and RA. This view is supported by overlapping serology characteristic of both diseases. It is also widely viewed as an erosive subset of SLE arthropathy[1].

Three popular view-points exist on the nature of rhupus. Some believe it to be a severe manifestation of arthritis in patients with SLE and different from an SLE/RA overlap. Others believe rhupus is a combination of SLE and erosive polyarthritis. The last group believe it is an overlap of RA and SLE (regardless to poly or oligoarthritis and erosive or non-erosive)[1,4-6].

With this definition the prevalence of rhupus has ranged from 0.09% by Panush *et al*[7] on evaluation of 7,000 new patients evaluated of whom they found six with both RA and SLE. The syndrome prevalence amongst systemic rheumatic disease is estimated to be between 0.01 and 2%[4,8].

Rhupus has been reported worldwide[5-10]. Simon and colleagues[8] described the clinical and immunological characteristics of Mexican patients with rhupus. Signs and symptoms of rheumatoid arthritis were present at the outset. There was little organic damage due to SLE without thrombi or pregnancy morbidities despite high anti-cardiolipin antibodies. They also had a high frequency of HLA-DR1 and HLA-DR2 alleles compared to controls. Sharman and colleagues[11] in Israel described three patients with rhupus and stressed the existence of progressive life threatening conditions such as APS, severe Raynauds syndrome with digital ulcers, pulmonary hypertension or malignancies.

Clinical features of lupus and RA overlap in the Rhupus syndrome. Eighty seven point nine percent exhibit swan neck deformities and non-erosive ulnar deviation. Skin rashes have been described in 30.7-71%, serositis (15.3-43%), neurological disorders (7-14%) and kidney involvement in (7-37.5%). RA associated features were also reported, erosions in the ulnar styloid, pseudocysts and joint space narrowing in 25% of cases[4,7,8].

There are variations in the clinical presentations of cases of lupus. Many initial cases selected in many series were patients who presented with features of RA who then developed features of SLE over an interval of 4.3 to 11 years[12]. Another study reported that 50% of rhupus cases were reported to be initially diagnosed as lupus, while 30% as arthritis and 20% were simultaneous presentations of both diseases[13]. Liu *et al*[14] reported that rhupus subjects with RA were reported to develop lupus after a mean interval of 9.2 years while those with lupus developed RA after a mean interval of 4.6 years.

Serologically there is the presence of Rheumatoid Factor (RF), anti-citrullinated peptide (anti- CCP), anti-nuclear and anti-collagen antibodies,

anti-Ro, anti-La, and anti-double stranded DNA. RF may occur in lupus patients with bone erosions (42-100%) and non-erosive arthropathy (10-33%). Other markers of erosive arthritis in rhupus patients include ESR, CRP and autoantibodies to type II collagen. Anti-CCP has been shown to increase the risk of erosive arthritis in patients with systemic lupus by 18 to 28 times. Other antibodies (ANA, SSA, SSB, anti-sm, anti-dsDNA and U1RNP occur in similar frequencies in erosive and non-erosive arthritis[15,16].

No specific cause has been determined for rhupus. Both lupus and rheumatoid arthritis are inflammation driven autoimmune disorders with strong genetic components. Genetic variations within the Major Histocompatibility Complex (MHC) have been well documented in cases of lupus and rheumatoid arthritis. Most rhupus patients (67%) have been shown to possess alleles of the share epitope while non erosive subjects do not. Simon *et al*[8] reported an increased prevalence of HLA-DR1, DR2, DR4 and DR6 alleles in distinguishing patients with rhupus. A significantly increased prevalence of HLA-DR1 and HLA-DR2 alleles was reported in Mexican patients with rhupus.

Little is known why patients with either lupus or rheumatoid transition occur concurrently. Hormonal, endocrine and immune mechanisms have been postulated. Environmental factors may play a role[17,18].

With increased awareness, it is anticipated that more of these cases will be reported from the African continent.

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