

Lupus, “Rhubus” and “Sjrupus”

To the Editor:

We offer the following comments on the recent article by Baer, *et al*¹.

Overlap of systemic lupus erythematosus (SLE) and Sjögren’s syndrome (Sj) certainly does occur and we are pleased that this has now been recognized and characterized. We wish to add our observations suggesting that this overlap, which we refer to as “sjrupus,” responds well to rituximab.

Patient 1. A woman who in 2000 at age 28 years developed autoimmunity characterized by sicca syndrome with positive SSA and SSB antibodies. There were lupus-like skin changes of discoid disease without SLE antibodies. Hydroxychloroquine (HCQ) was efficacious for arthralgia and later leflunomide was somewhat efficacious for lachrymal and salivary disease. In July 2005, coincidental with administration of Depo Provera, she developed severe bulky polysynovitis, lupus rashes on the face, malaise, and fatigue. Anti-dsDNA antibodies were off-scale positive along with SM, rheumatoid factor (RF) in IgA, M and G subclasses, SSA and SSB, but cyclic citrullinated peptide (CCP) antibodies were negative. Disease control required prednisone, adalimumab 40 mg weekly, leflunomide, parenteral methotrexate (MTX), and HCQ and we also tried mycophenolate mofetil. In 2006, rituximab was substituted and replaced all immunosuppressive drugs listed above, except HCQ. She was maintained on rituximab and HCQ alone. The result has been control of all clinical features of disease and she has regained lachrymal function such that she no longer needs artificial tears and her mouth is only mildly dry. To date she has been treated with 10 courses of rituximab over 48 months. Prior to rituximab and while taking prednisone, MTX, leflunomide, and adalimumab, her complement C’4 and C’3 were extremely low, but without abnormal urinalysis or renal dysfunction. Shortly after the first rituximab course, C’3 and C’4 returned to mid-normal and have remained normal. Since rituximab antibodies to dsDNA, Smith, and SSB have become negative, the RF has become negative in IgA and IgG, and the titer in IgM has decreased. ANA remains positive, titer 1:1280, homogenous pattern.

Patient 2. A woman who in 1999 at age 38 years developed fatigue, low grade fevers, polyarthrititis, and malar rash. Subsequent course has been one of remissions and relapses. Her only positive autoantibody is ANA, with a persistent mitotic spindle pattern; titer correlates with clinical disease activity. Sicca syndrome was noted early and gradually increased. Ophthalmologic cyclosporin A (Restasis) was also used. The entire disease was always responsive to prednisone. Addition of HCQ, leflunomide, MTX, and etanercept had benefit, but failed to fully prevent relapses. In 2008, rituximab was substituted for etanercept, MTX, and leflunomide and was clinically successful for fatigue, arthralgia, and sicca syndrome. Prednisone was tapered and discontinued. To date she has had 4 courses of rituximab and derives 5 months of relief of fatigue, sicca syndrome and arthrititis, fever, and rash from each infusion.

Patient 3. A man who in 2004 at age 40 years developed bulky polysynovitis, discoid lupus rashes, keratoconjunctivitis sicca, and dry mouth. His polysynovitis responded to adalimumab, but he suffered diverticulitis and adalimumab was discontinued. He returned in 2009 with severe bulky polyarthrititis and areas of skin atrophy and palor surrounded by red rims on the face, trunk, and extremities. Sicca syndrome continued and there was profound fatigue and Raynaud’s phenomenon. High-titer antibodies included RNP, Smith, ANA (fine speckled titer > 5120 on both mouse kidney and Hep-2 cells), RF in IgM, G and A, and anti-CCP antibodies. Tests were negative for antibodies to dsDNA, SSA, SSB, Scl-70, and centromere. Treatment with rituximab resolved the synovitis, fatigue, Raynaud’s phenomenon, and sicca syndrome. He has responded to 3 courses of rituximab over the past 12 months.

We suspect that when lupus overlaps with rheumatoid arthritis (RA) and Sjögren’s syndrome and also with Raynaud’s phenomenon, use of rituximab is efficacious and is sparing of multiple drugs with potential toxicities. Our Patient 1 is a startling example of absence of renal disease despite profound consumption of complement, supporting the observations of Baer, *et al* of lower frequency or renal disease in this overlap syndrome¹.

We also note there are increasing reports of successful treatment of Sjögren’s syndrome with rituximab. We have used rituximab to treat 22 patients with Sjögren’s syndrome for up to 53 months and as many as 11 courses. Two of these patients presented with salivary lymphoma. Analysis of responses of sicca syndrome, fatigue, and arthritis reveals significant improvement of all 3 indicators in 21 patients, and partial response in 1. Response was positive regardless of SSA and SSB antibody status and presence or absence of diagnosable RA and SLE. The response of Sjögren’s syndrome to rituximab has been also been confirmed prospectively².

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