Sjogren's Blog: July, 2009

Question: What are the options available for treatment of extraglandular manifestations of Sjogren's syndrome (SS)?

In this issue of the blog, I would like to ask our readers: **"What has been your experience in treating extra-glandular manifestations of SS?**

I am listing some of the "more common" extraglandular manifestations and drugs that we use at Scripps Memorial (La Jolla) in Table 1. I have not listed the specific references to each treatment, but they are available by Google scholar search for the disease manifestation and the therapy.

When I first started rheumatology training in Boston 25 years ago, I remember a series clinical "pearls" from my "gray bearded" attending. At first, these "pearls" seemed mutually incompatible, but over the years I have realized his wisdom. The first "pearl" was that "rheumatologists have only one drug—**prednisone**; and the art of rheumatology is how to avoid using it or to provide another medication to spare the patient steroids before he/she developed side effects."

The second "pearl" was "the best way to avoid or reduce medication side effects was not to prescribe the drug."

The final pearl was a question directed to the patients. "Don't like the side effects, how do you like those symptoms." As rheumatologists, these pearls outline our dilemma as we try to strike a balance between efficacy and toxicity. Further, some drugs come to market at doses that are "underdosed" or "overdosed" for a particular patient's manifestations—the problem is that we often don't know except by trial and error. Physician expertise, as shared in this blog, may help provide better care.

Most of our therapies for extraglandular manifestations in SS or in lupus are not "evidence-based," namely they have not been subjected to large-scale double-blinded studies. However, the series of case reports in SS suggest that the agents most useful in SLE will have a role in treatment of extraglandular manifestations of SS. In comparison, some of these agents (such as hydroxychloroquine, methotrexate, leflunomide or azathioprine) are also used in rheumatoid arthritis.

The extraglandular manifestations of SS (listed in Table 1) tend to fall in several categories:

a) vague fatigue and fibromyalgia; this is more than just a source of frustration for patient and rheumatologist—it has been the tail that wags the dog in therapeutic trials as we need to include both patient's and physician's global assessment of function.

b) immune complex disorders (vasculitis, pleurisy) and thrombotic disorders (including accelerated atherosclerosis and anti-coagulant mediated problems) similar to SLE; and

c) lymphocyte aggressive tissue infiltrations (ranging from interstitial pneumonitis, interstitial nephritis, neuropathies and lymphoproliferation straddling the border between pseudolymphoma and frank lymphoma).

The astounding success of TNF inhibition in RA patients was not duplicated in SS or SLE. Other biologics are still in trial but not yet officially approved. The "jury is still out" for rituximab in terms of multi-center double blind controlled trials.

However, I do not think we can ignore the many single center case reports in SLE and SS that have been published (and can be found using a Google scholar search) and particularly look for the response to rituximab for certain extra-glandular manifestations such as rash of mixed cryoglobulinemia, thrombocytopenia, certain neuropathies and "pseudolymphomas."

The data on biologics is less clear for ocular/oral dryness or even fatigue, but it seems that treatment with rituximab earlier in the disease may have more benefit than in later stages. However, in the current age of cost-control, it may be a difficult "sell" to insurance companies the expense of biologics for indications of dryness.

However, the finding of benefit of TNF inhibition in RA was largely unexpected and we may yet open the magic door for SLE and SS. We are still awaiting more data on anti-CD22 and anti-BAFF antibodies, as well as the anti-type I interferon and type I interferon receptor based on intriguing abstracts presented at last year's ACR.

However, there was little data on new therapies presented at EULAR this year, according to the abstracts presented on-line (http://www.abstracts2view.com/eular/sessionindex.php). So for now, we are still awaiting a magic bullet and perhaps so new hints at the next ACR meeting.

In this issue of the SS blog, I invite you to share your myths and pearls on therapy of extraglandular manifestations. Also, I would like your opinion of the published data.

Table 1 (available on my website robertfoxmd.com) presents a brief summary of agents used at Scripps in different extraglandular manifestations of SS that have been also reported on PubMed.