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Editorial

Axial Articular Manifestations in Primary Sjögren Syndrome: Have We Been Missing Spondyloarthritis for All This Time?

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Jarrot and colleagues[1] present a retrospective evaluation of 148 patients with primary Sjögren syndrome (SS) who fulfilled the American College of Rheumatology/European League Against Rheumatism criteria for SS, and also fulfilled the criteria for spondyloarthritis (SpA). The patients were largely from Marseille, France, and were followed over a prolonged time period.

The authors found symptoms suggestive of axial articular manifestation (AAM) in 29 patients (20% of all women in their SS cohort) in the cohort. Among the 29 patients that were chosen as AAM, 74% were found to have coexistent psoriatic arthritis and 26% ankylosing spondylitis (AS). These diagnoses were not immediately verified at the time of the initial diagnosis of SS. However, with longer follow-up and the persistence of back pain, the diagnosis of SpA was confirmed. Radiologic sacroiliitis was reported in 65% of the patients and HLA-B27 in 13% of the patients. Many (61%) of these patients with SS required biologic therapies with a good clinical response and no adverse effects on their SS.

The Jarrot, *et al*[1] study started from their observation of 3 patients in 2011 who had axial manifestations, which were later confirmed with a SpA diagnosis associated with their SS. One retrospective study in 2011 had reported a 0.6% prevalence of SpA in SS cohort[2]. However, this study did not report a follow-up on these patients, possibly leading to underdiagnosis of SpA, since the diagnosis of SpA can be delayed by several years.

In their discussion, Jarrot, *et al*[1] note one study from Turkey with a 25% prevalence of SpA in 85 SS patients (with 4% in age-matched controls)[3]. This study is published in the Pan African Medical Journal and references an increased coincidence of the two conditions in patients with ethnic origin in sub-Saharan Africa.

A PubMed search yields over 1000 hits for the search for "Sjögren's and sacroiliitis." The incidence in these publications generally ranges from 1% to 4%, which might be expected from the chance occurrence of two relatively frequent diseases. Thus, the much higher frequency in this study deserves a closer look.

Thus, two interesting questions unfold:

a. Why is the incidence of 20% of both SS and SpA in this cohort so much higher than we normally expect in our own clinics? Are we just not asking enough patients about back pain?

b. What are the interactions of genetic and environmental factors involved in this cohort? In a world with increased mobility of groups (as well as pathogens), do we need to be more alert regarding the ethnicity and travel habits of our patients?

Autoimmunity has frequently been attributed to the interaction of heredity (especially HLA) and environmental agents. Marseille, the second largest city in France, is described by *National Geographic* magazine as the "melting pot" of Europe and Africa. Indeed, so many lineages from Asia and Africa are found in Marseille, and attempts to sort out specific genotypes susceptible to a particular environmental agent may be difficult. For example, each particular genotype may have a particular articular type of reaction to a specific environmental agent[4].

In 2002, di Fazano, *et al*[5] reported of 13 cases of SS and SpA from a cohort of patients with sub-Saharan background. They suggested that the concurrence reflected the genetics and infectious diseases of that particular region of the world. African populations were still less mobile in their travel and in their marriage patterns outside of local ethnic groups. This would lead to maintenance of a more restricted pattern of HLA-B and HLA-DR antigens.

HLA-B27 is virtually absent in most of sub-Saharan Africa and AS is rare[5]. AS and HLA-B27 are more common in central and Southern Africa, but the incidence of SpA is actually lower than expected in these regions that used to be French colonies[5]. This would suggest that the environmental cofactor was encountered when the HLA-B27 individual moved from sub-Saharan Africa to Marseille.

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See Axial manifestations in SS, *page xxx*

In the study by Jarrot, *et al*[1], the Marseille patients initially presented with SS and later were diagnosed as having SpA. These patients with SS had genetic profiles showing HLA-DR associated with SS (information communicated by the authors). Since systemic lupus erythematosus (and extractable nuclear antigen–positive populations associated with the appropriate HLA-DR alleles) are known in sub-Saharan Africa[6], it seems likely that the genetic cofactor for SS was already present prior to the triggers for SpA.

However, the article by Jarrot, *et al*[1] also reminds us that we may not be asking enough patients about the symptoms of SpA. Patients get labeled with a particular disease such as SS and we may focus our increasingly limited time of revisit on that diagnosis alone.

In summary, Jarrot, *et al*[1] present the interesting features by a distinguished group of rheumatologists about the concurrence of SS and SpA, but it also reminds us about the genetic heterogeneity and how the choice of a "control" population cannot really serve as a comparator unless a "big data" approach is utilized. It is the conjecture of this editorial's author that an environmental agent that serves as a cofactor in SpA may have occurred as the HLA-B27 population (i.e., natives of the French empire in Africa) migrated to Europe. Also, this article reminds us to continually ask our SS patients about the development of other autoimmune conditions we do not normally associate with SS.

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