View Point

Does Spondyloarthritis Represent a Panel of Distinct Related Conditions or is it a single disorder with a Heterogeneous Phenotype?

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Spondylarthritis (SpA) is the second most prevalent form of chronic inflammatory arthritis[1]. The disease is characterized by inflammation as well as structural damage. The inflammation affects the spine and sacroiliac joint, the peripheral joints (with a predilection for large joints of the lower extremities), and extra-articular sites such as the eye, the gut, and the skin. The structural damage is dominated by new bone formation, although bone erosion can also be observed[2].

The phenotypic presentation of SpA is diverse and unpredictable, and therefore SpA has traditionally been subdivided into several subtypes, including ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), arthritis/spondylitis associated with inflammatory bowel disease (IBD), and undifferentiated SpA. This subclassification is mainly defined by the associated extra-articular features of the disease (psoriasis or IBD), pathogenesis (ReA), or outcome (AS).

However, all of the subtypes share similar axial (sacroiliitis/ spondylitis) or peripheral (arthritis, enthesitis, and/or dactylitis) articular manifestations. Moreover, a single patient with SpA can experience evolution from one subtype to another over time.

Therefore, classification according to the predominant rheumatic manifestations of axial and peripheral SpA was proposed in 1991 by the European Spondylarthropathy Study Group (ESSG)[3]. More recently, the Assessment of SpondyloArthritis international Society developed new classification criteria that go one step further than the ESSG criteria in subdividing the disease entity into axial SpA and peripheral SpA[4-6].

The phenotypic diversity of SpA and the different classification systems point toward a crucial question: does SpA represent a panel of distinct albeit related conditions, or is it a single multifaceted disorder?

It is obvious that a phenotypic sub-classification has major advantages for clinical research, including outcome research and clinical trials. However, phenotypic sub classification may also have major drawbacks, because it may obscure patho-physiologic research and limit the use of effective treatments to specific disease subtypes.

Disease should be primarily defined by its patho-physiology rather than by its phenotypic presentation. If the same cellular and molecular mechanisms are affecting different organs or tissues, as observed in systemic diseases such as systemic lupus erythematosus and sarcoidosis, the different phenotypes should be considered as belonging to a single disease. In contrast, specific phenotypes should be considered as distinct conditions if they are driven by clearly different pathologic mechanisms, as in Crohn's disease and ulcerative colitis in the IBD spectrum[7].

Accordingly, SpA subtypes should be reviewed according to the available and the current knowledge on the patho-physiology of its subtypes based on data from genetics, animal models, immuno-pathology, structural damage, and response to treatment.

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