Opinion

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Significance of Monocytes & Macrophages in Spondyloarthritis

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Opinion

Spondyloarthritis (SpA) is a collection of chronic inflammatory illnesses that mostly affect the spine and joints, with the sacroiliac joint being the most commonly implicated [1]. These diseases, which affect about 1% of the global population, cause serious ailments, suffering, disability, resulting in significant health and economical concerns [2]. In contrast to other rheumatic diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), the prevalence of spondylarthritis is equivalent in males and females, and the disease's beginning (third-fourth decade) occurs sooner than in other rheumatic joint diseases. The innate immune system cells are the initial line of defence against infections. Mucosal-associated invariant T (MAIT) cells, invariant natural killer T (iNKT) cells, gamma delta T cells (T cells), innate lymphoid cells (ILCs), neutrophils, mast cells, eosinophils, and monocytes and macrophages are among these cell types [3]. Monocytes and macrophages play an important role in the activation of the innate immune system, releasing inflammatory cytokines such as TNF, IL-6, IL-1, and chemokines after pathogen detection, which activate and attract other immune cells to the inflammation sites [4].

In the pathophysiology of SpA, a genetic relationship has been demonstrated. The strongest link was discovered in the HLA-B27 gene, which encodes the human leukocyte antigen (HLA) class I molecule 27 (HLA-B27), a key risk factor for the development of SpA, particularly AS and USpA [5]. Human leukocyte antigens (HLA), also known as Major Histocompatibility Complex (MHC), are in charge of presenting intracellular and extracellular peptides to immune system cells for activation. HLA-B27 is an MHC class I molecule that presents intracellular peptides to CD8+ T lymphocytes [6]. A number of epigenetic imbalances have also been linked to SpA development. Methylation is an important epigenetic mechanism involved in several illnesses, including SpA. Aberrant methylation is caused by an increase in the addition of methyl groups in specific gene regions. As a result, hypermethylation of promoter regions reduces gene expression, frequently exacerbating pathogenic symptoms [7]. In AS patients, GWAS studies revealed differentially methylation sites in the HLA-DQB1 gene. MicroRNAs (miRNAs) are also key epigenetic factors, and several studies have found that various miRNAs are dysregulated in SpA patients. One of the most significant studies discovered a pattern of 13 miRNAs unregulated in monocytes and 11 miRNAs deregulated in CD4+ T cells in patients with axSpA compared to controls, both of which are implicated in the pathogenesis of SpA. There are now several hypotheses that can coexist and all agree that the trigger for autoinflammatory processes is mediated by the HLA-B27 antigen. The first hypothesis holds that particular HLA-27 subtypes bind to peptides identified by CD8+ cells, activating autoreactive T cells [8].

The second hypothesis proposes that defective HLA-B27 folding at the endoplasmic reticulum of immune cells activates the unfolding protein response (UPR) pathway, which induces the translocation and thus activation of transcription factor NF-kB to the nucleus, resulting in the production of cytokines involved in disease pathogenesis by various inflammatory cells. Innate immune system cells are involved in the beginning and progression of SpA, and monocytes have been shown to play a critical role in the pathogenesis of these disorders. Monocytes are classified into three types based on the expression of the surface antigens CD14 and CD16. The most prevalent population, classical monocytes (approximately 90%), express high levels of CD14 but lack CD16 (CD14++ CD16-).Macrophages are innate immune system cells that are found in all tissues and body compartments and act as the initial line of defence against infection. They are the primary phagocytic cells, but they also serve as antigen presenters and release cytokines that aid in immune system activation. Macrophages are also important in the preservation of tissue homeostasis and in the orchestration of chronic inflammation seen in a variety of illnesses, including SpA.

Spondyloarthritis (SpA) refers to a group of chronic inflammatory illnesses, the most common of which are ankylosing spondylitis (AS) and psoriatic arthritis (PsA). These disorders share genetic, clinical, and immunological characteristics, such as the involvement of human leukocyte antigen (HLA) class I molecule 27 (HLA-B27), peripheral, spine, and sacroiliac joint inflammation, and the existence of extra-articular symptoms (psoriasis, anterior uveitis, enthesitis and inflammatory bowel disease).

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