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Chapter 1

Introductory Chapter: Introduction to Rheumatology

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1. Introduction

Rheumatology is a branch of science dealing with the different conditions that affect musculoskeletal tissues such as joints, bones, cartilage, tendons, ligament, and muscles. Rheumatism refers to various painful conditions that affect these tissues. Rheumatic diseases are those groups of diseases showing pain followed by reduction in the range of motion and function of musculoskeletal tissues. Arthritis is also one type of rheumatic disease referring to joint inflammation whether for joint pain, stiffness, inflammation, or joints damage. Most common types of rheumatic disease are rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) (Figure 1). The autoimmune diseases (such as RA, SLE, multiple sclerosis, and inflammatory bowel) have complex pathogenesis and multiple etiologies [1]. Studies have reviewed the role of various factors including genetic factors, epigenetic regulation, and environmental factors (such as cigarette smoking, crystalline silica, Epstein-Barr virus and reproductive hormones) in the pathogenesis of these autoimmune diseases [1]. There are many evidences showed that autoimmune diseases are multigenetic and their identification is associated with various types of genes [2]. There are a group of genes which induced the expression of proteins involved in various key pathophysiological pathways such as formation and clearance of immune complexes or apoptotic material, control of innate and adaptive immunity, production of immunological molecules like cytokines, chemokines, and adhesion molecules [3, 4]. Autoimmune patients have a great diversity in their genetic background and the nature of genes decides what kind of responsiveness is required to change the state of immune system [5]. There are various environmental factors that play an important role in these autoimmune diseases. These include infectious agents, ultraviolet (UV) light, and chemical or other compounds modifying immunological responses like environmental pollutants, drugs, or other behavioral habits such as smoking or diet [6, 7].
2. Systemic lupus erythematosus (SLE)

SLE is a multisystemic and complex autoimmune disease/condition characterized by loss of tolerance to self-antigens and production of high-titers serum autoantibodies with multifactorial etiology, which mainly affect women. The exact etiology of SLE is still unknown but there are various factors that might contribute to the onset of the disease and disease flare [8]. These include a number of environmental factors such as cigarette smoking, alcohol, chemicals and biochemicals, UV light, hormones, and infections caused by viruses, bacteria, and vaccine; all these contribute to induced lupus and disease flares [9]. These environmental factors trigger SLE by altering the epigenetic mechanism [10]. Epigenetic mechanisms which might trigger SLE include histone modification and DNA methylation, in which the cytosine base of DNA undergoes methylation and modification of histone tails including deacetylation, ubiquination, and tri-methylation [11]. In SLE, hypomethylation of DNA from CD4+ T cells takes place and as a result, T cells can function as autoreactive in response to self-class MHC II molecules [12].

UV light causes the main symptoms of SLE and triggers its onset [13]. This ability to induce this disease is dose related, meaning that more radiation causes greater severity in the disease [14]. If UV dose is low, normal apoptosis takes place in keratinocytes, while in high or moderate concentration, fragmentation of DNA, elevation in the expression of IL-1α, and necrosis of keratinocytes take place [14]. In conclusion, intermediate and high dose of UV light causes pro-inflammatory apoptosis and necrosis followed by the discharge of autoantigen and pro-inflammatory cytokines, which might trigger various inflammatory responses [14]. Smoking is also linked with increased risk of SLE and discoid lupus [15]. In addition to the relation between the risk of development of SLE and smoking, smoking is also associated with skin flares in patients with SLE [15]. Smoking also decreases the efficacy of antimalarials, but induces cutaneous lupus erythematosus [16]. No clear link has yet been established.
between the potential risk of SLE and alcohol consumption because the habit of smoking and alcohol often coexist, which interferes with the exact interpretation of the coexisting risk of development of SLE and alcohol habit [17]. One of the earlier studies has shown that neither past nor current alcohol consumption was associated with the development of SLE [18]. In an Internet-based study, it was found that current drinking habits are inversely associated with the development of SLE [19]. Certain medications are also known to induce lupus-like symptoms. Drug such as procainamide, which is an anti-arrhythmic drug, might induce lupus-like syndrome by acting as an inhibitor for DNA methyltransferase in human T cell lines [20]. Anti-TNF has been used in the treatment of inflammatory arthritis and is known to cause anti-TNF-induced lupus [21]. In addition, recent data suggest the role of estrogen and their metabolites in the pathogenesis of lupus [22–26].

3. Rheumatoid arthritis (RA)

Rheumatoid arthritis (RA) is a chronic inflammatory disorder in which inflammatory response develops especially in synovial joints. In this disease, the immune system mistakenly attacks our own body’s tissues. It affects mainly the lining of the joints and results in painful swelling of the joints that in turn results in bone erosion and causes joint deformity. The inflammation associated with the joints can damage the other parts of the body as well. There are various disorders associated with RA [27]. These include depression, fatigue, malaise, and anorexia. In addition to that, there are various complications including cardiovascular and hematologic complications, neurological problems, respiratory system disorders, and various other complications associated with RA. RA is found worldwide and affects nearly about 1% of the world population [28]. Women are more likely to have this disease, and it generally occurs at older age. Rheumatoid arthritis generally occurs at an age in between 30 and 50 years of age and its incidence varies among different populations. The actual cause of this disease is unknown but it is assumed that it probably occurs if a genetically susceptible host gets exposed to an environmental antigen [29]. This might generate immune response leading to the formation of various types of immune complexes, which generate inflammation in the joints. Recently, one study showed how inflammation occurs in joints of these rheumatoid arthritis patients [30]. Synovial cells produced high concentration of 16α-hydroxyestrone in rheumatoid arthritis patients. Despite normal concentration of 16α-hydroxyestrone in serum and urine, there is an elevated 16α-hydroxyestrone found in the synovial tissues, where activated immune cells are present. Therefore, 16α-hydroxyestrone combined with histone resulted in the formation of 16α-hydroxyestrone-histone adduct that might generate autoantibodies against this antigen. As a result, these autoantibodies trigger inflammation in the joints of RA patients [30]. Some studies also showed that viral or bacterial infections could act as potential environmental culprits to cause RA. Immunization with type II collagen also caused RA in experimental animals. Some patients of RA have shown that autoantibodies directed against heat shock proteins might show cross-reactivity with the bacterial antigen. There are numerous signs and symptoms associated with RA [31]. The most commonly affected joints in RA include fingers, feet, wrists, elbows, ankles, and knees. Shoulder, hip, and cervical spines are among those joints
that are affected later. The inflammation affects the joints to such an extent that these joints have pain during movement, swelling, and stiffness that last for hours. RA might also cause cardiovascular complications such as the development of acute necrotizing arteritis, thrombosis of the blood vessel leading to myocardial infarction, stroke or mesenteric insufficiency. Because RA mainly afflicts the joints, patients with RA should be encouraged to remain active and avoid heavy work [31]. Some exercises are recommended to maintain normal function of the joints and anti-inflammatory drugs are given to relieve from pain and swelling in the joints. Disease-modifying anti-rheumatoid drugs (DMARDS) should be given if the disease goes beyond 2 months. For mild conditions, hydroxychloroquine/minocycline is given, while for moderate disease, methotrexate followed by tumor necrosis factor (TNF) inhibitors is given.

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References


