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Systemic Lupus Erythematosus and Cardiovascular Disease

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Introduction

Systemic lupus erythematosus (SLE) is a challenging auto-immune disorder that incurs sporadic flares, remissions, and relapses (Robinson & Currie, 2011, p. 629). This auto-immune process is caused by the lack of tolerance to self-antigens within the adaptive immune system and can involve multiple organ systems, including the brain, heart and kidneys (Chen, Wu, Wang, Li, 2015, p. 1). SLE, also referred to as lupus, is a disease that affects women more often than men, especially during their childbearing years (Robinson & Currie, 2011, p. 631). Over the past 3 decades, the five-year survival rate for patients suffering from Lupus have increased from 50% to 95% with decreasing deaths from infection and renal disease (Weinstein et al., 2014, p. 130). Cardiovascular disease, however, continues to be a main cause of death for those diagnosed from SLE (Gilbert & Ryan, 2014, p. 1902). The cardiovascular system is known to be a potential target for patient with lupus, causing 7- to 10-fold increase in cardiovascular disease (CVD) (Weinstein et al., 2014, p. 130). Complications of CVD include pericarditis, valvular and atherosclerotic changes. Women with SLE, however, are unaware of the increased risk of cardiovascular disease associated with lupus (Weinstein et al., 2014, p.130).

SLE can be masked by the signs and symptoms of other superficial disease processes, while the underlying etiology is auto-immune (Weinstein, 2012, p. 38). Understanding the pathophysiology of SLE can aid in early diagnosis and treatment to provide better long-term patient outcomes and improve quality of life.

Signs & Symptoms

SLE can be difficult to diagnose as many symptoms are vague and non-specific, such as fatigue, joint pain, fever and recurrent infections. Females are at a higher risk of developing SLE than males by a 9:1 ratio (Weinstein, 2012, p. 39). Currently, there is no formal diagnostic test for SLE, however, the American College of Rheumatology have developed a list of criteria to help diagnose patients with lupus.

Four of the following symptoms must be present for the formal diagnosis of Lupus (Weinstein, 2012, p. 39):

- Malar Rash
- Discoid Rash
- Photosensitivity
- Oral ulcers
- Arthritis
- Serositis
- Persistent protein in the urine
- Seizures or psychosis
- Blood disorders: anemia, leukopenia, lymphopenia, thrombocytopenia
- Immunologic disorders: positive anti-double-stranded DNA (anti-dsDNA), anti-Sm, antiphospholipid antibodies (aPL)
- Positive antinuclear antibody (ANA) test

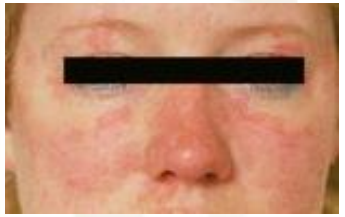

Figure 1. Malar Rash

Pathophysiology

The pathophysiology of SLE occurs at both the cellular and tissue level. The cellular level refers to the production and tolerance of auto-antibodies. The clinical manifestations of SLE occur at the tissue level by the formation of immune complexes that accumulate and deposit in organ tissues.

Cellular level.

- Abnormal activation of T and B cells, along with altered signaling events within the cell are characteristic in those with SLE (Tsokos, 2011, p. 2111).
- Signaling abnormalities within the cell lead to a deficiency of the interleukin-2 (IL-2) cytokine, causing a decrease in efficacy of the cytotoxic T-cell and a decrease in apoptosis of the auto-reactive T cells (Tsokos, 2011, p. 2111).
- T cells migrate to inflamed areas of the body and have a heightened expression of the CD44 adhesion molecules, facilitating attachment to the endothelial lining of the blood vessel (Tsokos, 2011, p. 2112).
- Plasma cells are responsible for antibody production and are increased during the active stage of SLE (Tsokos, 2011, p. 2112). An increased production of auto-reactive antibodies correlates to the expression/flares of SLE.
- The immune response is limited/controlled by the expression of Treg cells. Patients with SLE have decreased and/or dysfunctional Treg cells, which contribute to the pathogenesis of SLE (Moulton & Tsokos, 2015, p. 2224).

Tissue level.

- SLE is referred to as a type III hypersensitivity with the production of immune complexes that are deposited into peripheral tissues. Immune complexes are composed of multiple auto-antibodies and self-antigens that are circulating within the blood stream (Liao, Reihl, & Luo, 2016, p. 1).
- Once the immune complexes are deposited into the tissues, the compliment system is activated which ultimately instigates the innate inflammatory response and promotes tissue damage (Liao, Reihl, & Luo, 2016, p. 1).

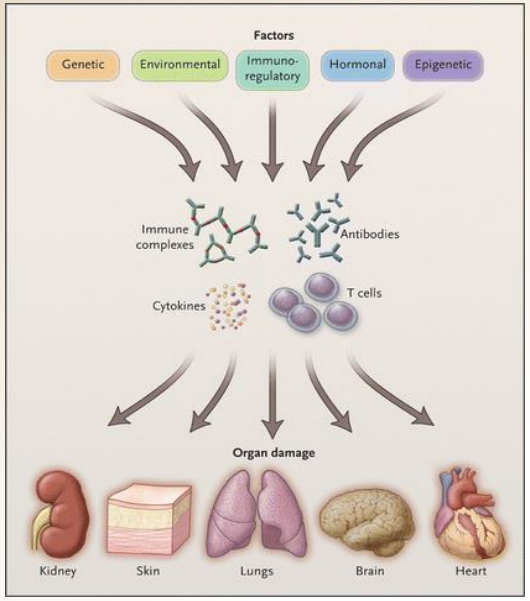

Figure 2. Pathophysiology of SLE (Tsokos, 2011, p. 2112)

Significance of Pathophysiology

- According to the CDC (2015), prevalence and incidence rates for SLE are difficult to predict due to the non-specific nature of presenting symptoms. Prevalence rates have varied in the United States from 161,000 to 1.5 million cases. Family history is a strong predictive value for development of lupus with more than 20 different genetic abnormalities identified (Weinstein, 2012, p. 40).
- Auto-antibodies in patients with SLE are thought to be the initial causative agent associated with endothelial damage (Turano, 2013, p. 50). Several different auto-antibodies have been identified in the pathogenesis of SLE, including anti-dsDNA, antiphospholipid (aPL), anti-Sm and ANA (Weinstein, 2012, p. 42).
- Overexpression of antibody adhesion molecules promotes endothelial damage, leading to atherosclerosis (Tsokos, 2011, p. 2112). The extent of atherosclerosis is directly correlated to the duration of SLE symptoms (Turano, 2013, p. 49)
- Epigenetic changes can alter the functionality of T cells and instigate the auto-immune response in SLE (Moulton & Tsokos, 2015, p. 2225). According to Moulton & Tsokos (2015), hypomethylation of numerous genes, including CD11A, perforin, CD70, and CD40L, have been implicated in the development of SLE (p. 2225).
- The focus of treatment is associated with limiting the effect of inflammation on local tissues to prevent damage with non-steroidal anti-inflammatory drugs (NSAIDS), corticosteroids, antimalarial and immunosuppressive agents (Turano, 2013, p. 49).

Implications for Nursing Care

Understanding the pathophysiology of auto-immune disorders, such as SLE, aids in the screening, diagnosis and early treatment to decrease the progression of SLE. Using solely the traditional Framingham risk factors for cardiovascular disease in patients with SLE is ineffective in providing appropriate preventative therapy (McMahon et al., 2014, p. 131).

Healthcare professionals should screen for cardiovascular risk factors in patients with SLE, including (Turano, 2013, p. 51):

- Hypertension
- Dyslipidemia
- Diabetes Mellitus
- Obesity
- SLE disease activity
- Renal function
- Antiphospholipid or lupus anticoagulant levels

Preventative screenings provide better identification of high risk patients and enable early preventative care. In addition, education should be provided to all patients regarding the risk of cardiovascular disease. Focus should be placed upon modifiable risk factor management of blood pressure, weight, smoking status, and activity level.

Treatment using aggressive blood pressure management should be maintained in patients with SLE. Use of a multi-drug regimen, including angiotensin-converting enzyme (ACE) inhibitors, and thiazide diuretics, may be necessary to control hypertension (Turano, 2013, p. 52). The use of beta-blockers can precipitate Raynaud's phenomenon in patients with SLE and should be utilized only as a second-line treatment (Turano, 2013, p. 51). Corticosteroids are considered to be the gold standard treatment in SLE. Long-term use of corticosteroids, however, increases the risk of developing insulin resistance and obesity, thereby, increasing the risk of cardiovascular disease (Turano, 2013, p. 51). Utilizing individualized plans of care better tailor treatment to each patient with SLE, improving the efficacy of treatment and prolonging the progression of SLE.

Conclusion

Systemic Lupus Erythematosus is difficult to diagnose as many symptoms are non-specific, including fatigue, joint pain and fever (Weinstein, 2012, p. 38). A comprehensive history and physical assessment should be performed by a healthcare practitioner to determine possible risk for SLE (Weinstein, 2012, p. 39). Early screening and diagnosis, as well as, appropriate risk factor management strategies have improved long-term patient outcomes. Progressive treatment plans for patients with SLE has improved life expectancy and quality of life (Turano, 2013, p. 48). Cardiovascular disease and atherosclerosis are becoming the leading cause of death amongst patients with SLE and have been attributed to the new successful treatment options and improved life expectancy (Gilbert & Ryan, 2014, p. 1902). Healthcare providers should focus on patient education regarding increased risk for cardiovascular disease associated with SLE and risk factor management (Weinstein, Amirkhosravi, Angelopoulos, Bushy, Covelli & Dennis, 2014, p. 137).

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