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Etiology and Pathogenesis of Systemic Lupus Erythematosus

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Abstract:

Systemic lupus erythematosus (SLE) is an immunopathogenic complex disease that affect many organs of the body. Several pathogenic mechanisms have been identified. Inspite of the new knowledge about understanding the exact mechanisms and triggering parameters for SLE, the exact etiology has not been identified yet. A combination between many factors and complex reactions secondary to different genetic and environmental factors is supposed to be involved. different genes are implicated in disease activity. An abnormal immune cascade triggered by the combination ofhormonal and environmental factors or some drugs or chemicals leads to abnormal immune complexes, which are important contributors to the development of SLE. certain environmental factors are supposed to be needed to trigger the disease. activation of both B cells and T cells and other immune cells and leads to activation of the immune mechanism. SLE is heterogeneous in presentation, which may affect one organ only or had a multisystem effect, with varying clinical presentations ranging from mild cutaneous manifestations to severe multiorgan affection or severe central nervous system affection. This makes the diagnosis and management of SLE very challenging. Management so SLE is determined according to the organ involved and the severity of the disease.

Keywords: pathogenesis, genetic, interaction, Systemic lupus erythematosus.
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Introduction:

SLE is an immune disease that affects many parts of the body, the exact etiology of it is not well understood. However, several theories are supposed to be the cause of the disease as gene polymorphism, immunopathogenic factors, endocrinal factors, and abnormal environmental factors play a role in the etiology of SLE.(1)

Many authors tried to search the etiology and pathology of SLE trying to reach if there is a preventable factor. The conclusion until now is that the etiology is multifactorial of many factors interacting together resulting in triggering abnormal immune responses resulting in the abnormal and unregulated production of autoantibodies and cytokines leading to the deposition of immune complexes in tissue and leading to organ damage.(2) ZThe widespread release of antibodies and the deposition of immune complexes, complement activation, by activation of a both innate and adaptive immune response, and result in generalized tissue affection and multiorgan damage manifesting of SLE.(3)

1- Genetic factors*:*

As the disease is noticed that it may

run in families and has a very high rate of occurrence in identical twins, play a role in understanding the rule of genetic factors in SLE, although there is no clear or specific genetic pattern. Many studies reported that the disease rates for identical twins may reach to be up to 60%. Many genes identified to be accused with polymorphisms have been reported to be associated with SLE . and also many monogenic forms of SLE have been identified. (4)

These genes are associated with the expre-ssion of abnormal immune response and activation of the abnormal and unregulated and uninhibited immune cascade that finally results in immune complex deposition and organ damage. Some gene mutations may cause the development of SLE and activation of both B and T cells immune response.(5)

Some of the other genes associated include HLA-DRB1, HLA-DR2, HLA-DR3, HLA-DRX, etc. the site of these genes is the major histocompatibility (MHC) locus. The MHC contains genes for antigen-presenting molecules. The expression of these genes or gene mutations is the accused cause and carries a very high risk for the appearance of the disease.(6)

The high prevalence of SLE in females more than in males may lead o the unde-rstandingthat there is an association with genes on the X-chromosome. However, the exact genes have not been identified although much research was made hoping to identifyit. (7)

2- Hormonal factors

The hormonal effect is one of the major and significant risk factors for SLE. Female sex hormones such as Estrogen stimulates innate and specified immune cells that cause the release of some specific cytokines and activation of autoantibodies and the expression of HLA. It is well known that estrogens and prolactin increase the rate of antibodies production from the B-cells , and activation of dendritic cells, and complement system activation. (8)

The use of contraceptives containing estrogen and have been reported to be associated with higher rates of SLE and increased incidence of lupus flares, this effect also have been reported with the use of hormone replacement therapy and in patients with high prolactin levels. On the other hand, elevated androgens levels are associated with lower rates of the disease. (9)

Researches have proven that estrogens increase the incidence of SLE, while androgens play an immunosuppressive effect by antagonizing the effects of estrogen. Moreover, the hormonal on SLE activity is matching the findings that the disease activity and flares increase during the period of puberty and pregnancy or with using estrogen hormonal therapy.(10)

3- Environmental factors

many environmental factors implicated in triggering SLE have been described. Ultraviolet rays and sun exposure can increase the incidence of the disease and may increase disease activity by increasing cell apoptosis. Also, exposure to some chemicals and industrial materials and hot weather may act as triggers for SLE.(11)

4- drugs

Many drugs have been supposed to cause SLE-like manifestations as procainamide and hydralazine Also the sulfa-drugs have been reported to be associated with flares in patients with SLE.(12)

5- Infections

Many viral infections have been shown to increase the risk of SLE, and the explanation is reported to be antibody similarity. Epstein-Barr virus (EBV) antibodies are more common

in patients with SLE in comparison to the general population. [13]

Conclusion

The underlying pathogenesis of SLE is complex and multifactorial and the understanding of the etiology of SLE is constantly evolving. Many factors are implicated together in triggering the disease and more research is needed for determining the exact mechanism hoping to reach for the preventive strategy that can stop disease activity inpredisposed patients.

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