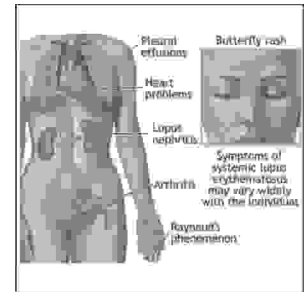


REVIEW

PROF-1331

LUPUS**MISS. NAGEEN HUSSAIN**

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ABSTRACT... nageen1704@hotmail.com Lupus is an autoimmune disorder in which the immune system becomes hyperactive; results in the formation of auto-antibodies that react with the “self” antigens to form immune complexes. These immune complexes build up in the tissues; can cause inflammation, injury to tissues, pain and bring about the symptoms^{1,2}. Systemic Lupus Erythematosus (SLE) is one of the type of lupus which affects multiple organ systems and is multifactorial in etiology^{2,3}.

Key words: Lupus, auto-antibodies, inflammation, immune complexes, Systemic Lupus Erythematosus.

INTRODUCTION

Lupus is the Latin word for wolf and Erythematosus means redness; it is so-called because the skin lesions resemble the bite of a wolf³. The cause of lupus is unknown, but genetic, non-genetic and immunological factors are there. The fundamental defects in SLE seem to be a failure to maintain self-tolerance; as a consequence, a wide array of autoantibodies are produced that damage tissues⁴. The cellular and molecular basis of autoimmunity in SLE is still not clear¹.

SLE is a common autoimmune disease; its incidence may be as high as one case per 2500 persons in certain populations. It is three times more common in Africans and in Americans than in Caucasians. It occurs in all races and ages but is more common in young adult women; therefore it is also known as “woman’s disease”⁵.

Etiology

Genetic Factors: Genes on chromosome 1 and chromosome 6 are associated with lupus in certain families^{6,7}. In North American Caucasian populations, there is positive association between SLE and class II HLA genes particularly at the HLA-DQ locus^{7,8}.

The importance of genetic factors in the etiology of autoimmune diseases is evident from the fact that these disorders tend to cluster in families. The identical twins are more likely to develop the same autoimmune disease than the fraternal twins and close relatives of patients with Lupus are at higher risk of developing the same or a different autoimmune disease⁹.

Immunological Factors: B-cell hyperactivity is a feature of SLE. It is believed that CD4⁺ Helper T-cells drive self-reactive B-cells to make auto-antibodies. The

mechanisms by which T-cells lose self tolerance are still unknown; however, it is clear that the basis of immunologic dysregulation is multifactorial¹⁰.

Some lupus patients have inherited deficiencies of complement components. Lack of complement, impairs the removal of immune complexes from the circulation, and favors tissue deposition and thus cause tissue injury¹¹.

Environmental Factors: Some of the environmental factors that may trigger the disease are;

Infections
Antibiotics
Ultraviolet light
Extreme stress
Certain drugs
Hormones

Gender is also an important contributory factor in the development of Lupus. Approximately 8% of the general population is affected by autoimmune diseases and about 78% of these are females¹.

Sex hormones have an important influence on the development of SLE. Androgen appears to protect and estrogen seems to influence the development of SLE¹⁴. Hormonal factors may explain why lupus occurs more frequently in females than in males. The increase of disease symptoms before menstrual periods or during pregnancy support the belief that hormones, particularly estrogen, may somewhat regulate the way the disease progresses. However, the exact reason for the greater prevalence of lupus in women, and the cyclic increase in symptoms, is unknown¹⁵.

The importance of microbial infection as a trigger for the induction of systemic lupus erythematosus is frequently debated. Clinical observations indicate that anti-viral and antibacterial responses are often accompanied by self reactivity, and anti-pneumococcal antibodies elicited in non-autoimmune individuals by pneumococcal vaccine express lupus-associated anti-DNA idiotypes^{16,17}.

TYPES

There are four types of lupus:¹⁸

1. Cutaneous Erythematosus:
2. Systemic lupus erythematosus
3. Drug-induced lupus
4. Neonatal lupus

1. Cutaneous Lupus Erythematosus

Cutaneous Lupus Erythematosus most often affects young adult women aged 20 to 50. It can be provoked by sunlight and is more common in dark skinned than in fair skinned people. Such people have circulatory problems. If they are smokers or living in a cool climate then they may suffer from Raynaud's phenomenon in which there is abnormal blanching of fingers and toes. Mild arthritis of finger joints may also occur¹⁹.

a. **Chronic Cutaneous Lupus** is also known as discoid lupus. Here rashes appear in the form of coin or oval shaped especially on those area of the skin that are exposed to sunlight such as butterfly rash over the face, V of the neck, back of the hands. These rashes leave scar or the skin get discolored. It may be localized or widespread^{5,19}.

* LE tumidus is a non-specific presentation of cutaneous LE which is very rare. Papules, plaques and nodules come up on the cheeks, upper chest, upper arms or back. This is so called because on skin biopsy, deposits of mucin are detected in the dermis^{18,19}.

* Lupus profundus is also known as 'lupus panniculitis' affecting the fat underlying skin. The face is the most common area to be affected. The end result is unsightly dented scars fat cells that are completely destroyed by the lupus^{4,5}.

* Rarely discoid lupus erythematosus occurs on the palms and soles called Palmoplantar discoid lupus¹⁹.

b. **Acute lupus erythematosus** refers to a typical malar eruption in a butterfly pattern localized to the central portion of the face²⁰.

c. **In Subacute LE**, a non-itchy dry rash appears on the upper back and chest, often following sun exposure but does not leave the scar. It includes the following clinical types:²¹.

- * Annular or polycyclic
- * Papulosquamous
- * Vasculitis
- * Nodular

Photosensitivity is one of the most common manifestations of lupus erythematosus. In these patients, there is a relationship between exposure to ultraviolet light, autoantibodies, genetics and other factors in the development of photosensitivity. The basis for photosensitivity in lupus has yet to be fully defined. It is more commonly associated with subacute and tumid lupus erythematosus than with other variants².

2. Systemic lupus erythmatosus

Systemic lupus erythmatosus is a non-organ- specific autoimmune disease which affects multiple organ systems like skin, joints, kidney, heart, blood vessels⁷. Immunologically, the disease involves an array of antibodies against DNA, RNA, Phospholipids, histone, and collagen. SLE is a very serious, usually incurable and often fatal disease because of the production of these different anti-self antibodies^{5,14}. The clinical presentation of SLE is so variable and bears so many similarities to other autoimmune connective tissue diseases that it has been necessary to develop diagnostic criteria (table I) . The diagnosis of SLE is established when the patient fulfill four out of eleven of these criteria^{23,24}.

3. Drug Induced Lupus

There are different drugs that are capable of triggering the onset of systemic lupus erythematosus such as procainamide, isoniazid, thorazine etc.

Table-I. The revised criteria for the classification of SLE: (Tan et al 1982).

| |
|---|
| Butterfly rash |
| Discoid lupus |
| Photosensitivity |
| Oral ulcer |
| Arthritis |
| Serositis: Pleuritis, pericarditis |
| Renal disorder: proteinuria, cellular cast |
| Neurological disorder, seizures, psychosis |
| Hemopoietic disorder, (hemolytic anemia, leucopenia, lymphopenia, thrombocytopenia) |
| Immunological disorder |
| Abnormal titer of anti-nuclear antibody |

Table-II.

| |
|--|
| Class I: Normal by light, electron and immunoflourescent microscopy which is quite rare. |
| Class II: Mesangial lupus glomerulonephritis |
| Class III:Focal glomereulonephritis |
| Class IV: Diffuse proliferative glomerulonphritis |
| Class V: Membranous glomerulonephritis |

Around 1 patient per 1,000 treated with such a drug gets the temporary lupus, the symptoms of which almost always disappear when the person stops taking the drug. There is some interesting evidence about what these different drugs have in common, including some inhibition of DNA methylation^{24,25}.

4. Neonatal Lupus

Fifty percent of the women with SLE complete nine months of pregnancy normally. 25% of them deliver baby normally and the remaining 25% face miscarriage or fetal death. The term neonatal lupus is used to describe major symptoms found in newborns. The most common

symptom is a rash that is usually scattered over the body, not necessarily on the face. It shows up a few days or weeks after birth, particularly after sun exposure, and usually disappears after a few more weeks, leaving no scar. The second commonest symptom is an abnormal blood count: low platelets, anemia, and other abnormalities. Neonatal lupus is not the same as adult lupus such babies do not develop arthritis, fever, and kidney or brain disease²⁶.

Cognitive Dysfunction: People with mild to moderately active SLE describe the feelings of confusion, fatigue, memory impairment and difficulty in expressing their thoughts. Such symptoms are collectively known as cognitive dysfunction. Lupus headache is very similar to migraine and is common in Raynaud's phenomenon²⁷.

Morphology

The morphological changes in SLE result largely from the formation of immune complexes in a variety of tissues as a result of which many organs get involved².

1. **Skin lesions:** Skin lesions are prominent clinical findings in these patients; they are usually exhibited by exposure to sunlight or ultraviolet light^{19,20,21}.
2. **Kidney involvement** is one of the most important anatomic features of SLE and renal failure is an important cause of death. According to the world health organization morphologic classification, five patterns are recognized (Table II)²⁸.

| Diseases (Values in%) | dsDNA | Histone | SS-A | SS-B | Sm | RNP/Sm |
|-----------------------|-------|---------|-------|-------|-------|--------|
| SLE | >90 | 30-50 | 10-30 | 10-50 | 10-30 | 10-30 |
| Drug induced Lupus | - | 50-90 | - | - | - | - |
| Raynaud's phenomenon | 10-30 | - | - | - | - | >90 |
| Sjogren's syndrome | 10-30 | - | >90 | >90 | - | - |

The pathogenesis of all forms of glomerulonephritis involves deposition of DNA- antiDNA complexes within the glomeruli².

Cardiovascular system involvement is manifested in the form of pericarditis²⁹.

Serosal membranes particularly the pericardium and pleura may exhibit a variety of changes ranging from serious effusion to fibrous a pacification.

Joint involvement is clinically very important, when present; it consists of swelling and a non-specific mononuclear cell infiltration in the synovial membrane¹⁴.

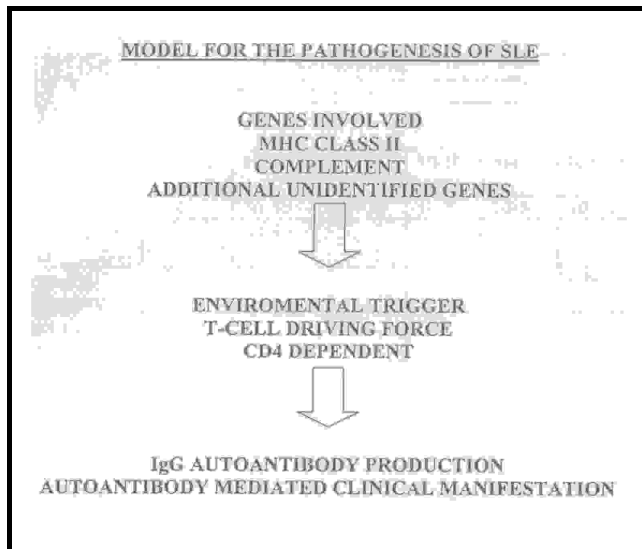
Central Nervous System involvement is common. Neuronal damage may be caused by antineuronal

antibodies^{30,31}.

Diagnosis: Diagnosis is usually made by a careful review of a person's entire medical history coupled with an analysis of the results obtained in routine laboratory tests and some specialized tests related to immune status. Systemic lupus is difficult to diagnose for a number of reasons:^{18,32,33}

- * Systemic lupus is a multi-system disease.
- * It is a disease that does not typically develop rapidly, but rather develops slowly and evolves over time.
- * Systemic lupus is known as a "Great Imitator" because it mimics so many other diseases and conditions.
- * Systemic lupus is difficult to diagnose because

there is no single diagnostic test for lupus.



Antiphospholipid antibodies are present in 30% to 40% of lupus patients and react with a wide variety of anionic phospholipids. Therefore, these antibodies are sometimes referred to as "lupus anticoagulant". The pathogenesis of thrombosis in patients with antiphospholipid antibodies is unknown proposed mechanism include direct endothelial cell injury, antibody mediated platelet activation and inhibition of endogenous anticoagulants such as protein C. A term Primary antiphospholipid syndrome is used in which patients don't have necessarily the symptoms of SLE but possess lupus anticoagulants^{34,35}.

Treatment: Long lasting inflammation results in lupus so the treatment is to reduce inflammation. Support groups, counseling, talking to family members, friends, and physicians can help alleviate the effects of stress. Medications are often prescribed for people with lupus, depending on which organs are involved, and the severity of involvement. Commonly prescribed medications include: Non-steroidal Anti-inflammatory Drugs, Acetaminophen, Corticosteroids, Antimalarials, Immunomodulating Drugs, and Anticoagulants³⁶.

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