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A Review on Systemic Lupus Erythematosus

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ABSTRACT:
Lupus is a chronic inflammatory autoimmune disease. There are four main types of lupus: neonatal, discoid, drug-induced, and systemic lupus erythematosus (SLE). Systemic lupus erythematosus (SLE) is a multisystem inflammatory disease characterized by highly varied clinical manifestations in association with antinuclear antibody (ANA) production. This disease occurs primarily in young women especially in childbearing age and ranges in the severity from a mild disease with rash and arthritis to a devastating illness with renal failure and nervous system disturbances. Because of the variability in the course of SLE, the approach to therapy is individualized for each patient and is determined by the array of clinical manifestations. The medication most commonly used to control the lupus.

KEY WORDS: Lupus, systematic lupus erythmatosus, symptoms, manifestations, diagnosis, treatment.

I. INTRODUCTION:

Lupus is a chronic inflammatory autoimmune disease caused when the immune system attacks it own tissues. There are four main types of lupus: neonatal, discoid, drug-induced, and systemic lupus erythematosus (SLE). In this type of SLE affects the majority of patients. Patients with lupus has a loss of self-tolerance as a result of abnormal immunological function and the production of auto antibodies, which lead to the formation of immune complexes that may adversely affect healthy tissue of person. Systemic lupus erythematosus (SLE) can affect persons of all ages and both sexes, but more than 90% of patients presenting with SLE are women in the childbearing years.

Lupus is associated with multi systemic inflammation resulting from abnormal immunological function. Patients has periodic flares of varying severity, and inflammation caused by lupus can affect the different body system like-joints, skin, brain, kidney, heart, lungs and blood cells.

TYPES:

Drug induced lupus:

Drug induced lupus (DIL) caused by certain prescription of drugs.DIL occurs after exposure to a medications, causing an autoimmune response. Various organ systems are affected by DIL, but clinical manifestations usually subside upon discontinuation of the responsible agent.

DIL is induced by minocycline, a semi synthetic tetracycline are frequently used in the treatment of acne vulgaris, rheumatoid arthritis and other inflammatory conditions. Minocycline induced lupusoccurs mostly in young patients.

Symptoms are muscle and joint pain, fever, occasionally pleuritis and pericarditis are develops aside effect of long term medication. DIL refers to an idiosyncratic side effect of numerous, unrelated medication in which symptoms overlap with those of SLE.

Discoid lupus erythematosus:.

Discoid lupus erythematosus is a chronic dermatological disease that can lead to scarring, hair loss, and hyper pigmentation changes in skin .The cause is thought to be genetic, with the highest prevalence in women, African-Americans, and persons between 20 and 40 years of age. It is diagnosed by biopsy of a rash on the scalp, face, neck, or arms.

In some cases histopathology may be required to confirm the diagnosis. Early recognition and treatment improves the prognosis. Potent topical steroids, antimalarial drugs and immunosuppressive agents like azathioprine, cyclosporine, mycophenolatemofetil, and methotrexate are used in the treatment.

Neonatal lupus erythematosus:

Neonatal lupus erythematosus (NLE) observed in newborns, NLE is thought to result from maternal auto-antibodies passing through the

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placenta. However, pediatric patients who have positive maternal auto-antibodies, only about 1% develop NLE. Common clinical presentations involve the heart, liver, and skin. Significant morbidity and mortality, along with cardiac manifestations, have been noted.

NLE refers to a clinical spectrum of cutaneous, cardiac, and systemic abnormalities observed in newborn infants whose mothers have auto-antibodies against Ro/SSA, La/SSB, and, less commonly, U1 ribonucleoprotein (U1-RNP). The infants may have no skin lesions at birth but develop them during the first weeks of life. Cardiac, hematological, hepato biliary, central nervous and pulmonary systems may also be involved. The condition is usually benign and self-limited but sometimes may be associated with serious conditions.

Systemic lupus erythematosus [SLE]:

The immune system normally fights against dangerous infections and bacteria to keep the body healthy. An autoimmune disease occurs when the immune system attacks the body tissues because it confuses it for something foreign. There are many autoimmune diseases, including systemic lupus erythematosus (SLE). The term lupus has been used to identify a number of immune diseases that have similar clinical presentations and laboratory features.

SLE is commonly referred as "lupus" but it is differentiated from other types by its multi-organ system effects. It may affect male and female especially in childbearing age. SLE is more commonly observed in African-Americans, Asians, Hispanics, and Native Americans.SLE is the most common form of lupus, comprising 70% of lupus cases. It is a systemic condition. This means that it can affect multiple organs in the body. For this reason, SLE tends to be a more severe form of lupus. The symptoms can range from mild to severe.SLE patients are able to live a normal life with treatment.

CAUSES OF SYSTEMIC LUPUS ERYTHEMATOSUS

Causes of SLE is unknown, there are several factors associated with the development of SLE. Genetic, hormonal, immunological, and environmental factors all play a role in the development of SLE. SLE patients do not clear apoptotic cells appropriately. These cells release auto-antigens that may helps to drive the defective immune process. The complex interaction between environment and immunologic factors in genetically susceptible individuals leads to continued deregulation of the innate and adaptive immune pathways with evidence of auto-antibody secreting plasma cells and auto-antigen, hyper-reactive, memory B-cells. Auto-antibodies often form long before clinical manifestations result in chronic, widespread tissue and organ damage.

Immunology:

Immunological involvement in SLE focuses on a patient's loss of "self-tolerance". Phagocytosis process is compromised in SLE patients, leading to the inappropriate removal of apoptotic cells and immune complexes. SLE is the formation of auto antibodies that go to form immune complexes in combination with antigens leading to inflammation and tissue damage.

Environment:

Environmental factors include certain viruses and ultra - violet (UV) light. UV light stimulates keratinocytes, leading to B-cell stimulation and antibody production; it may also stimulate T-cell activity, resulting in additional autoantibody production. Epstein–Barr virus (EBV) has also been linked to the SLE in children. Smoking, silica, and some hair products (e.g., dyes) may also be possible triggers of lupus.

Genetic factors:

Due to genetics Lupus is being more common in certain demographics. However, differences in certain outcomes. Strongest association of one of the chromosome regions with SLE is the human leukocyte antigen (HLA) locus, mainly the class region containing HLA- DRB1, DQA1 and -DQB1. There are also associations of some of these loci with specific clinical and serological features. Most of the Evidence suggests that there is a higher chance of a person developing lupus if a family member has it, further supporting the possibility that genetics may be a risk factor. There is a higher prevalence of SLE in the African-Caribbean population living in Europe and North America, compared with the Caucasian population. Twin studies also used to show that if a member of identical twins has lupus, the other has a 24% chance of also developing the disease.

Predictors:

The laboratory tests used to predict a SLE flare (particularly lupus nephritis) is an increasing serum level of anti-DNA antibodies and a fall in

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complement levels (especially C3). Approximately 50–60% of patients will experience a flare, with 10% of this group experiencing a severe flare. The leading causes of death in the first decade of disease are systemic disease activity, renal failure, infections and thrombo embolic events. Subsequently, atherosclerosis and cancer become more common causes of death.

Organ dysfunction:

SLE can affect every organ and system in the body, and during the flares more than one organ is affected like ocular, thrombosis, renal, gastrointestinal, cutanaceous, hematological, neurological, cardio pulmonary. Disease activity is categorized into mild forms, moderate and severe. Mild disease is clinically stable with no life-threatening condition. Patients with moderate disease activity have more serious manifestations, such as cutaneous vasculitis or pericarditis, and severe disease activity is defined as life threatening.

SYMPTOMS:

The symptoms of lupus occur in times of flare-ups, between flare-ups, people usually experience times of remission, when there are few symptoms. The main symptoms are cutaneous, gastrointestinal, cardiovascular, renal, articular, hematological or pulmonary, fatigue, memory problems, joint pain, leg edema, skin bleeding, pneumonia, thrombosis, Reynaud's disease, arthritis. In addition, the disease may be acute and severe with high fever. SLE is most common in females than in males, but the cause of this sexual preference is notestablished.

Symptoms in female

- Chest pain
- Sensitivity to sunlight
- Mouth ulcer
- Arthritis
- Malar rash

Symptoms in male

- cardiovascular complications
- low blood count
- weight loss
- kidney problems
- chest pain

MANIFESTATIONS OF SLE:

Constitution manifestation:

The patients with SLE may present with various systemic manifestations. The general symptomsinclude:

- Fever
- Malaise
- Arthralgia
- Myalgia
- Headache
- Loss of appetite & weight

Weight gain due to corticosteroid treatment or active disease such as nephrotic syndrome. These symptoms can mimic other autoimmune diseases, infectious diseases, endocrine abnormalities, chronic fatigue, and fibromyalgia.

Musculoskeletal manifestation:

Involvement of the musculoskeletal system is common in patients with SLE. Patients most often seek medical attention for joint pain, with small joints of the hand and wrist usually affected. Arthralgia, arthritis, osteonecrosis (avascular necrosis of bone), and myopathy are the principal of manifestations. Arthritis and arthralgia have been noted in upto 95% of patients with SLE. The arthritis of SLE is generally considered to be non-deforming. Osteoporosis often due to glucocorticoid therapy may increase the risk of fractures. Some SLE patients have myositis that can be proved by biopsy.

Dermatological manifestation:

SLE comprises four diagnostic criteria:

- Malar rash which is characterized by an erythematous rash over the cheeks and nasal bridge. It lasts from days to weeks and is occasionally painful.
- The second feature is photosensitivity, which may be elicited from patients who are asked if they have any unusual rashes or symptoms after the sun exposure.
- The third feature may be discoid rash. Discoid lesions often also develop in sun exposed areas but are plaque like in character, with follicular plugging and scarring. They may be part of systemic lupus or may represent discoid lupus without organ involvement, which is a separate diagnostic entity.
- Alopecia is the fourth and often less-specific cutaneous feature of SLE. It often affects the temporal regions or createa patches like hair loss.

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Renal manifestations:

The kidney is the most commonly involved organ in SLE. Approximately 50% of patients with SLE develop renal disease, biopsy studies to demonstrate the renal involvement in all patients. In general, lupus nephritis occurs in more than half of SLE patients. Lupus nephritis is primarily caused by the deposition of immune complexes. The classification of lupus nephritis is based on renal biopsy. A biopsy should be obtained in any patient in whom renal involvement is suspected. Renal biopsy is not be done routinely in patients with normal creatinine values and normal urine analysis.

Neuropsychiatric manifestations:

Neurological manifestations of lupus are reported in 25 to 75% of patients and can involve all parts of the nervous system. SLE may be generalized or partial and may precipitate status epileptics. Aseptic meningitis, myelopathy, optic neuropathy, or other demyelinating disorders may also require urgent evaluation. Stroke and transient ischemic attack (TIA) may be related to antiphospholipid antibody syndrome or vasculitis. Migraine headaches may also be linked to antiphospholipid syndrome, although this is less clear. Headache and mood disorders may be the most commonly reported neurologic manifestation of SLE, but cause and effect may be difficult.

Pulmonary manifestations:

Pulmonary manifestations of SLE may manifest acutely. It may represent many complications. Serositis can affect both the cardiac and pulmonary systems.Cardiac and pulmonary serositis often coexist. . SLE Patients may get chest pain on inspiration, most commonly in the form of pleurisy. This can be due to lupus activity, pulmonary embolism or secondary infection, so needs careful investigation to define the causes. Pulmonary hypertension without underlying parenchymal lung disease rarely occurs with symptomatic dyspnea or right-sided heart failure. Thromboembolic disease associated with antiphospholipid antibodies can lead to acute pulmonary embolism with acute pulmonary hypertension. Much rarer pulmonary manifestations include active lupus pneumonitis, pulmonary haemorrhage and pulmonary hypertension. Pulmonary hypertension is associated with a poor prognosis, especially in pregnancy.

Gastro intestinal manifestations:

The most common gastrointestinal manifestation of SLE is oral ulceration. Gastrointestinal symptoms are common in patients with SLE due to primary gastrointestinal disorders.

Abnormalities of liver function not included in the diagnostic criteria of SLE, and generally liver is not a major target organ for damage in patients with SLE. Hepatitis from lupus is uncommon, manifests as a mild elevation in liver enzymes (aspartate transaminase [AST], alanine transaminase [ALT], lactate dehydrogenase [LDH], alkaline phosphatase), usually in a setting of active lupus. Mostly 50% of patients suffering abdominal pain, nausea, vomiting or diarrhea at some stage of disease, although side effects of therapeutic interventions will contribute some of those symptoms. The most serious gastrointestinal complication of SLE is enteric vasculitis.

Cardiac manifestations:

The premature coronary artery disease is associated with inflammatory conditions like SLE was recognized. The preventative medication that reflects this increased risk of SLE and particularly it is associated with hypercholesterolaemia. Autoimmune vascular injury in SLE may predispose to atherosclerotic plaque. An increased incidence of risk factors for atherosclerosis has been noted. Heart failure or chest pain carefully examined in patients with SLE. Pericarditis is most common symptomatic cardiac manifestation of SLE and Myocarditis is less common SLE, it may be associated with arrhythmia and heart failure.

Vascular manifestations:

There is few information on its vascular manifestations. Patients with SLE can develop inflammatory vascular disease in the form of vasculitis. Vasculitis in SLE is due to a complex between immune cells, endothelial cells, deposition of autoantibodies, and immune complexes. There have also been reports of SLE and Takayasu's arteritis (a rare type of vaculities, that cause blood vessel inflammation).

Occular manifestations:

The most common ocular manifestation of SLE is keratoconjunctivitis sicca (KCS), occurring in approximately of 25% of patients. Retinal involvement in SLE is the second most common ocular manifestation after KCS. Conjunctivitis, interstitial keratitis, episcleritis, and diffuse or nodularscleritis are less common. The neuro

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ophthalmological manifestations of SLE are associated with brain and optic nerve damage, then may be caused ischemic process. It should be carefully evaluated for systemic involvement to detect potentially treatable and preventable complications of those patients associated with ocular lupus disease.

Endocrine manifestation:

Thyroid dysfunction is most frequent in SLE patients than the general population and it may have a genetic basis, 3-24 % of patients with lupus have autoimmune thyroid disease. Type 1 and Type 2 diabetes mellitus is not common in patients with lupus. Vitamin D deficiency is common in SLE due to avoidance of sun exposure. Prolonged glucocorticoid used to suppress the pituitary function.

Hematologic manifestation:

Patients with SLE have a abnormalities of immune system. A history of multiple cytopenias such as leukopenia, lymphopenia, anemia, or thrombocytopenia may suggest SLE, among other etiologies. Leukopenia and lymphopenia are common in SLE, and this hypocomplementemia may predispose persons with SLE. Anemia is mostly occur in young menstruating women. Thrombocytopenia may be mild or part of a thrombotic thrombocytopenic purpura (TTP)–like antiphospholipid antibody syndrome (APS).

DIAGNOSIS OF SLE:

Systemic lupus eythematosus is a multisystem inflammatory disease that is difficult to diagnose. SLE is diagonised by its signs and symptoms, laboratory testing, and diagnostic testing to each patient. Anti nuclear antibody titer is the primary laboratory test used to diagnose in SLE. Because of the lower prevalence of the disease in primary care populations, the antinuclear antibody titer has a low predictive value in patients without typical clinical symptoms. Diagnostic laboratory analyses include a complete blood count (CBC), a complete metabolic profile, and a urinalysis to determine the creatinine clearance and the presence of proteinuria or active sediment is commonly performed. Radiography can be used to assess joint involvement, renal ultrasound, kidney size and impairment, chest radiography, pulmonary involvement, and electrocardiography, chest pain.

TREATMENT;

Treatment for lupus depends on your signs and symptoms. The medications most commonly used to control the lupus include:

Nonsteroidal anti-inflammatory drugs (NSAIDs): NSAIDs, such as naproxen sodium and ibuprofen used to treat pain, swelling and fever associated with lupus. Side effects of NSAIDs may include stomach bleeding, kidney problems and increased risk of heart problems.

Antimalarial drugs: Medications commonly used to treat malaria, such as hydroxychloroquine affect the immune system and can help to decrease the risk of lupus flares. Side effects can include stomach upset and very rarely damage to the retina of the eye. Regular eye examination is recommended when taking these medications.

Corticosteroids: Prednisone and other types of corticosteroids are used in the inflammation of lupus. High doses of steroids such as methyl prednisolone are used to control the serious disease that involves kidneys and brain. Side effects may include weight gain, easy bruising, thinning bones, high blood pressure, diabetes and increased risk of infection. Higher doses and longer term therapy to increase the risk of side effects.

Immuno suppressants: Drugs that used to suppress the immune system in serious cases of lupus. Examples include azathioprine, mycophenolate, methotrexate, cyclosporine and leflunomide. Potential side effects are increased risk of infection, liver damage, decreased fertility and anincreased risk of cancer.

Biologics: The aim of biologics is to control the specific molecular targets is anticipated for the treatment of systemic lupus erythematosus (SLE). Belimumab was the first biological approved for SLE. At present, many biologicals such as anifrolumab and ustekinumab are in clinical trials. Belimumab administered intravenously, it reduces the lupus symptoms in some people. Successful treatments with biologicals targeting "bridging cytokines" produced by dendritic cells, which form a bridge between the innate and acquired immune systems. Side effects include nausea, diarrhea and infections. Rarely depression can occur. Other potential drugs to treat lupus are currently being studied, including abatacept, anifrolumab and others.

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II. CONCLUTION:

Lupus has a wide range of symptoms that may affect the people in different ways. Some people may experience cycles of flare-ups and remissions, whereas others may have ongoing symptoms. The varied experiences of lupus can make it challenging for doctors to diagnose. However, once a doctor has diagnosed the condition, there are several treatments that can manage a person's symptoms and limit damage to their organs. No cure has been discovered for this autoimmune disease, many medications are available to help control flares, to maintain remission, and to manage symptoms. Pharmacists and other health care professionals can play a vital role in treatment by educating patients, monitoring their therapeutic regimens, and identifying preventable drug-associated adverse events. Current research is under way, with the hope that improved quality of life and increased survival can be achieved for the many patients affected by SLE each year.

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