Systemic Lupus Erythematosus: A Review

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Summary

Systemic lupus erythematosus often abbreviated to SLE or lupus, is a systemic autoimmune disease that can affect any part of the body. This article deals with basic fundamentals about this autoimmune disease, the epidemiology, the pathology of the disease, the sign and symptoms of the disease, the current therapy available and scope of research in this field.
Keywords: - Systemic lupus erythematosus, autoimmune diseases, epidemiology, pathology.

1. Introduction

Systemic lupus erythematosus often abbreviated to SLE or lupus, is a systemic autoimmune disease (or autoimmune connective tissue disease) that can affect any part of the body. As occurs in other autoimmune diseases, the immune system attacks the body's cells and tissue, resulting in inflammation and tissue damage.[1] It is a Type III hypersensitivity reaction caused by antibody-immune complex formation. The course of the disease is unpredictable, with periods of illness (called flares) alternating with remissions. The disease occurs nine times more often in women than in men, especially in women in child-bearing years ages 15 to 35, and is also more common in those of non-European descent.[2] [3]. Survival for people with SLE in the United States, Canada, and Europe has risen to approximately 95% at five years, 90% at 10 years, and 78% at 20 years, [3] and now approaches that of matched controls without lupus.

2. Etymology

There are several explanations ventured for the term lupus erythematosus. Lupus is Latin for wolf, [4] and "erythro" is derived from Greek for "red." All explanations originate with the reddish, butterfly-shaped malar rash that the disease classically exhibits across the nose and cheeks.

1. In various accounts, some doctors thought the rash resembled the pattern of fur on a wolf's face.
2. In other accounts, doctors thought that the rash, which was often more severe in earlier centuries, created lesions that resembled wolf bites or scratches.

3. Another account claims that the term "lupus" did not come from Latin directly, but from the term for a French style of mask that women reportedly wore to conceal the rash on their faces. The mask is called a "loup," French for "wolf."

3. Epidemiology

The rate of SLE varies considerably between countries, ethnicity, gender, and changes over time.[5] In the United States the prevalence of SLE is estimated to be about 13 per 100,000, translating to about 159,000 out of 300 million people in the US being affected.[5][6] In Northern Europe the rate is about 40 per 100,000 people. SLE occurs more frequently and with greater severity among those of non-European descent. That rate has been found to be as high as 159 per 100,000 among those of Afro-Caribbean descent.[5]

4. Pathophysiology

One manifestation of SLE is abnormalities in apoptosis, a type of programmed cell death in which aging or damaged cells are neatly disposed of as a part of normal growth or functioning.

5. Transmission

In SLE, the body's immune system produces antibodies against itself, particularly against proteins in the cell nucleus. SLE is triggered by environmental factors that are unknown. "All the key components of the immune system are involved in the underlying mechanisms [of SLE]" according to Rahman, and SLE is the prototypical autoimmune disease. The immune system must have a balance (homeostasis) between being sensitive enough to protect against infection, and being too sensitive and attacking the body's own proteins (autoimmunity). From an evolutionary perspective, according to Crow, the population must have enough genetic diversity to protect itself against a wide range of possible infection; some genetic combinations result in autoimmunity. The likely environmental triggers include ultraviolet light, drugs, and viruses. These stimuli cause the destruction of cells and expose their DNA, histones, and other proteins, particularly parts of the cell nucleus. Because of genetic variations in different components of the immune system, in some people the immune system attacks these nuclear-related proteins and produces antibodies against them. In the end, these antibody complexes damage blood vessels in critical areas of the body, such as the glomeruli of the kidney; these antibody attacks are the cause of SLE. Researchers are now identifying the individual genes, the proteins they produce, and their role in the immune system. Each protein is a link on the autoimmune chain, and researchers are trying to find drugs to break each of those links. [7] [8]. SLE is a chronic inflammatory disease believed to be a type III hypersensitivity response with potential type II involvement. Reticulate and stellate acral pigmentation should be considered a possible manifestation of SLE and high titers of anticardiolipin antibodies, or a consequence of therapy.[9][10]

Abnormalities in apoptosis:

- Apoptosis is increased in monocytes and keratinocytes
- Expression of Fas by B cells and T cells is increased
- There are correlations between the apoptotic rates of lymphocytes and disease activity.

Tingible body macrophages (TBMs) – large phagocytic cells in the germinal centers of secondary lymph nodes – express CD68 protein. These cells normally engulf B cells that have undergone apoptosis after somatic hypermutation. In some people with SLE, significantly fewer TBMs can be found, and these cells rarely contain material from apoptotic B cells. Also, uningested apoptotic nuclei can be found outside of TBMs. This material may present a threat to the tolerization of B cells and T cells. Dendritic cells in the germinal center may endocytose such antigenic material and present it to T cells, activating them. Also, apoptotic chromatin and nuclei may attach to the surfaces of follicular dendritic cells and make this material available for activating other B cells that may have randomly acquired self-specificity through somatic hypermutation.[10]. SLE, like many autoimmune diseases, affects females more frequently than males, at a rate of almost 9 to 1.[73] The incidence of SLE in the United States increased from 1.0 in 1955 to 7.6 in 1974. Whether the increase is due to better diagnosis or to increasing frequency of the disease is unknown.[11]

6. Signs and symptoms of SLE

The American College of Rheumatology established eleven criteria in 1982, which were revised in 1997 as a classificatory instrument to operationalise the definition of SLE in clinical trials. They were not intended to be used to diagnose individuals and do not do well in that capacity. For the purpose of identifying patients for clinical studies, a person has SLE if any 4 out of 11 symptoms are present simultaneously or serially on two separate occasions. [12]

1. Malar rash (rash on cheeks); sensitivity = 57%; specificity = 96%.[13]
2. Discoid rash (red, scaly patches on skin that cause scarring); sensitivity = 18%; specificity = 99%.[13]
3. Serositis: Pleurisy (inflammation of the membrane around the lungs) or pericarditis (inflammation of the membrane around the heart); sensitivity = 56%; specificity = 86% (pleural is more sensitive; cardiac is more specific).[13]
4. Oral ulcers (includes oral or nasopharyngeal ulcers); sensitivity = 27%; specificity = 96%.[13]
5. Arthritis: nonerosive arthritis of two or more peripheral joints, with tenderness, swelling, or effusion; sensitivity = 86%; specificity = 37%.[13]
6. Photosensitivity (exposure to ultraviolet light causes rash, or other symptoms of SLE flareups); sensitivity = 43%; specificity = 96%.[13]
7. Blood—hematological disorder—hemolytic anemia (low red blood cell count) or leukopenia (white blood cell count<4000/µl), lymphopenia (<1500/µl) or thrombocytopenia (<100000/µl) in the absence of offending drug; sensitivity = 59%; specificity = 89%.[13] Hypocomplementemia is also seen, due to either consumption of C3 and C4 by immune complex-induced inflammation or to congenitally complement deficiency, which may predispose to SLE.

8. Renal disorder: More than 0.5 g per day protein in urine or cellular casts seen in urine under a microscope; sensitivity = 51%; specificity = 94%.[13]
9. Antinuclear antibody test positive; sensitivity = 99%; specificity = 49%.[13]
10. Immunologic disorder: Positive anti-Smith, anti-ds DNA, antiphospholipid antibody, and/or false positive serological test for syphilis; sensitivity = 85%; specificity = 93%.[13] Presence of anti-ss DNA in 70% of cases (though also positive with rheumatic disease and healthy persons).[54]
11. Neurologic disorder: Seizures or psychosis; sensitivity = 20%; specificity = 98%.[13]

The signs and symptoms of SLE can be explained by the figure: 1

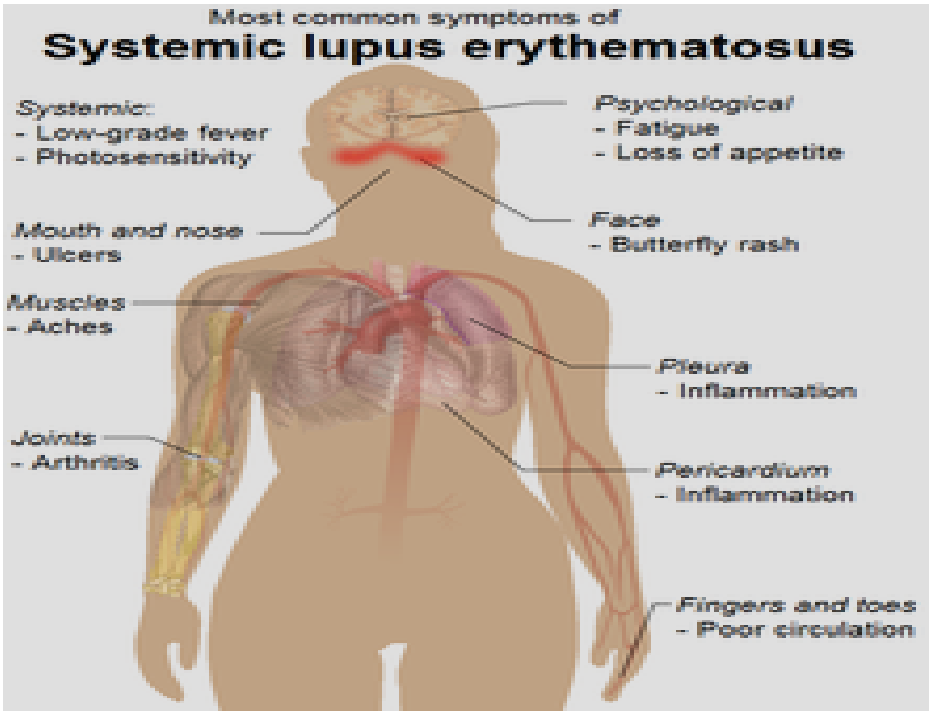

Figure: 1

SLE is one of several diseases known as "the great imitators" because it often mimics or is mistaken for other illnesses. SLE is a classical item in differential diagnosis,[2] because SLE symptoms vary widely and come and go unpredictably. Diagnosis can thus be elusive, with some people suffering unexplained symptoms of untreated SLE for years. Common initial and chronic complaints include fever, malaise, joint pains, myalgias, fatigue, and temporary loss of cognitive abilities. Because they are so often seen with other diseases, these signs and symptoms are not part of the diagnostic criteria for SLE.

7. Dermatological manifestations

As many as 30% of sufferers have some dermatological symptoms (and 65% suffer such symptoms at some point), with 30% to 50% suffering from the classic malar rash (or butterfly rash) associated with the disease. Some may exhibit thick, red scaly patches on

the skin (referred to as discoid lupus). Alopecia; mouth, nasal, urinary tract and vaginal ulcers, and lesions on the skin are also possible manifestations. Tiny tears in delicate tissue around the eyes can occur after even minimal rubbing.

8. Musculoskeletal manifestations

The most commonly sought medical attention is for joint pain, with the small joints of the hand and wrist usually affected, although all joints are at risk. The Lupus Foundation of America estimates more than 90 percent of those affected will experience joint and/or muscle pain at some time during the course of their illness. Unlike rheumatoid arthritis, lupus arthritis is less disabling and usually does not cause severe destruction of the joints. Fewer than ten percent of people with lupus arthritis will develop deformities of the hands and feet. SLE patients are at particular risk of developing osteoarticular tuberculosis. [14][15]. A possible association between rheumatoid arthritis and SLE has been suggested,[10] and SLE may be associated with an increased risk of bone fractures in relatively young women.[16]

9. Hematological manifestations

Anemia may develop in up to 50% of cases. Low platelet and white blood cell counts may be due to the disease or a side effect of pharmacological treatment. People with SLE may have an association with antiphospholipid antibody syndrome[12] (a thrombotic disorder), wherein autoantibodies to phospholipids are present in their serum. Abnormalities associated with antiphospholipid antibody syndrome include a paradoxical prolonged partial thromboplastin time (which usually occurs in hemorrhagic disorders) and a positive test for antiphospholipid antibodies; the combination of such findings have earned the term "lupus anticoagulant-positive". Another autoantibody finding in SLE is the anticardiolipin antibody, which can cause a false positive test for syphilis. [17]

10. Cardiac manifestations

A person with SLE may have inflammation of various parts of the heart, such as pericarditis, myocarditis, and endocarditis. The endocarditis of SLE is characteristically noninfective (Libman-Sacks endocarditis), and involves either the mitral valve or the tricuspid valve. Atherosclerosis also tends to occur more often and advances more rapidly than in the general population.[18][19][20]

11. Pulmonary manifestations

Lung and pleura inflammation can cause pleuritis, pleural effusion, lupus pneumonitis, chronic diffuse interstitial lung disease, pulmonary hypertension, pulmonary emboli, pulmonary hemorrhage, and shrinking lung syndrome

12. Renal manifestations

Painless hematuria or proteinuria may often be the only presenting renal symptom. Acute or chronic renal impairment may develop with lupus nephritis, leading to acute or end-stage renal failure. Because of early recognition and management of SLE, end-stage renal failure occurs in less than 5% of cases. A histological hallmark of SLE is membranous glomerulonephritis with "wire loop" abnormalities. This finding is due to immune complex deposition along the glomerular basement membrane, leading to a typical granular appearance in immunofluorescence testing.

13. Neuropsychiatry manifestations

Neuropsychiatry syndromes can result when SLE affects the central or peripheral nervous systems. The American College of Rheumatology defines 19 neuropsychiatry syndromes in systemic lupus erythematosus.[21] The diagnosis of neuropsychiatry syndromes concurrent with SLE is one of the most difficult challenges in medicine, because it can involve so many different patterns of symptoms, some of which may be mistaken for signs of infectious disease or stroke.[22]

The most common neuropsychiatry disorder people with SLE have is headache,[23] although the existence of a specific lupus headache and the optimal approach to headache in SLE cases remains controversial.[24] Other common neuropsychiatry manifestation of SLE include cognitive dysfunction, mood disorder, cerebrovascular disease,[23] seizures, polyneuropathy,[23] anxiety disorder, and psychosis. It can rarely present with intracranial hypertension syndrome, characterized by an elevated intracranial pressure, papilledema, and headache with occasional abducens nerve paresis, absence of a space-occupying lesion or ventricular enlargement, and normal cerebrospinal fluid chemical and hematological constituents.[25]. More rare manifestations are acute confusional state, Guillain-Barré syndrome, aseptic meningitis, autonomic disorder, demyelinating syndrome, mononeuropathy (which might manifest as mononeuritis multiplex), movement disorder (more specifically, chorea), myasthenia gravis, myelopathy, cranial neuropathy and plexopathy.

14. Neurological manifestations

Neural symptoms contribute to a significant percentage of morbidity and mortality in patients with lupus.[26] As a result, the neural side of lupus is being studied in hopes of reducing morbidity and mortality rates.[21] The neural manifestation of lupus is known as neuropsychiatric systematic lupus erythematosus (NPSLE). One aspect of this disease is severe damage to the epithelial cells of the blood-brain barrier. Lupus has a wide range of symptoms which span the body. The neurological symptoms include headaches,[23] depression, seizures, cognitive dysfunction, mood disorder, cerebrovascular disease,[23] polyneuropathy, anxiety disorder, psychosis, and in some extreme cases, personality disorders. In certain regions, depression reportedly affects up to 60% of women suffering from SLE.[27]

15. Reproductive manifestations

SLE causes an increased rate of fetal death in utero and spontaneous abortion (miscarriage). The overall live-birth rate in SLE patient has been estimated to be 72%.[28] Pregnancy outcome appears to be worse in SLE patients whose disease flares up during pregnancy.[29] Neonatal lupus is the occurrence of SLE symptoms in an infant born from a mother with SLE, most commonly presenting with a rash resembling discoid lupus erythematosus, and sometimes with systemic abnormalities such as heart block or hepatosplenomegaly.[29] Neonatal lupus is usually benign and self-limited.[29]

16.Systemic manifestations

Fatigue in SLE is probably multifactorial and has been related to not only disease activity or complications such as anemia or hypothyroidism, but also to pain, depression, poor sleep quality, poor physical fitness and perceived lack of social support.[30] [31]

17. Causes

There is no one specific cause of SLE. There are, however, a number of environmental triggers and a number of genetic susceptibilities.[32][33]

18. Genetics

The first mechanism may arise genetically. Research indicates SLE may have a genetic link. SLE does run in families, but no single causal gene has been identified. Instead, multiple genes appear to influence a person's chance of developing lupus when triggered by environmental factors. The most important genes are located in the HLA region on chromosome 6, where mutations may occur randomly (de novo) or may be inherited. HLA class I, class II, and class III are associated with SLE, but only classes I and II contribute independently to increased risk of SLE.[34] Other genes which contain risk variants for SLE are IRF5, PTPN22, STAT4,[35] CDKN1A,[36] ITGAM, BLK,[35] TNFSF4 and BANK1.[37] .Some of the susceptibility genes may be population specific.[35]

19. Environmental triggers

The second mechanism may be due to environmental factors. These factors may not only exacerbate existing SLE conditions, but also trigger the initial onset. Researchers have sought to find a connection between certain infectious agents (viruses and bacteria), but no pathogen can be consistently linked to the disease. Some researchers have found that women with silicone gel-filled breast implants have produced antibodies to their own collagen, but it is not known how often these antibodies occur in the general population, and there are no data that show these antibodies cause connective tissue diseases such as SLE. There is also a small but growing body of evidence linking SLE to lipstick usage.[38] [39] [40]

20. Drug reactions

Drug-induced lupus erythematosus is a (generally) reversible condition that usually occurs in people being treated for a long-term illness. Drug-induced lupus mimics SLE. However, symptoms of drug-induced lupus generally disappear once the medication that triggered the episode is stopped. More than 38 medications can cause this condition, the most common of which are procainamide, hydralazine, quinidine, and phenytoin.[2]

21. Non-SLE forms of lupus

Discoid (cutaneous) lupus is limited to skin symptoms and is diagnosed by biopsy of rash on the face, neck, scalp or arms.

22. Diagnosis

Antinuclear antibody (ANA) testing and anti-extractable nuclear antigen (anti-ENA) form the mainstay of serologic testing for SLE. Several techniques are used to detect ANAs. Clinically the most widely used method is indirect immunofluorescence. The pattern of fluorescence suggests the type of antibody present in the patient's serum. ANA screening yields positive results in many connective tissue disorders and other autoimmune diseases, and may occur in normal individuals. Subtypes of antinuclear antibodies include anti-Smith and anti-double stranded DNA (dsDNA) antibodies (which are linked to SLE) and anti-histone antibodies (which are linked to drug-induced lupus). Anti-dsDNA antibodies are highly specific for SLE; they are present in 70% of cases, whereas they appear in only 0.5% of people without SLE.[2] The anti-dsDNA antibody titers also tend to reflect disease activity, although not in all cases.[2] Other ANA that may occur in SLE sufferers are anti-U1 RNP (which also appears in systemic sclerosis), SS-A (or anti-Ro) and SS-B (or anti-La; both of which are more common in Sjögren's syndrome). SS-A and SS-B confer a specific risk for heart conduction block in neonatal lupus.[41]. Other tests routinely performed in suspected SLE are complement system levels (low levels suggest consumption by the immune system), electrolytes and renal function (disturbed if the kidney is involved), liver enzymes, and complete blood count.

The lupus erythematosus (LE) cell test was commonly used for diagnosis, but it is no longer used because the LE cells are only found in 50–75% of SLE cases, and they are also found in some people with rheumatoid arthritis, scleroderma, and drug sensitivities. Because of this, the LE cell test is now performed only rarely and is mostly of historical significance.

23. Treatment

The treatment of SLE involves preventing flares and reducing their severity and duration when they occur. Treatment can include corticosteroids and anti-malarial drugs. Certain types of lupus nephritis such as diffuse proliferative glomerulonephritis require bouts of cytotoxic drugs. These drugs include cyclophosphamide and mycophenolate. Hydroxychloroquine (HCQ) was the last medication approved by the FDA for lupus in

1955.[42] Some drugs approved for other diseases are used for SLE 'off-label'. In November 2010, an FDA advisory panel recommended approving Benlysta (belimumab) as a treatment for the pain and flare-ups common in lupus. The drug was approved by the FDA in March 2011.

24. Medications

Due to the variety of symptoms and organ system involvement with SLE, its severity in an individual must be assessed in order to successfully treat SLE. Mild or remittant disease may, sometimes, be safely left untreated. If required, nonsteroidal anti-inflammatory drugs and antimalarials may be used. Medications such as Prednisone, Cellcept and Prograf have been used in the past. A number of potential treatments are in clinical trials.

25. Disease-modifying antirheumatic drugs

Disease-modifying antirheumatic drugs (DMARDs) are used preventively to reduce the incidence of flares, the process of the disease, and lower the need for steroid use; when flares occur, they are treated with corticosteroids. DMARDs commonly in use are antimalarials such as plaquenil and immunosuppressants (e.g. methotrexate and azathioprine). Hydroxychloroquine is an FDA-approved antimalarial used for constitutional, cutaneous, and articular manifestations. Hydroxychloroquine has relatively few side effects, and there is evidence that it improves survival among people who have SLE. Cyclophosphamide is used for severe glomerulonephritis or other organ-damaging complications. Mycophenolic acid is also used for treatment of lupus nephritis, but it is not FDA-approved for this indication, and FDA is investigating reports that it may be associated with birth defects when used by pregnant women.

26. Immunosuppressive drugs

In more severe cases, medications that modulate the immune system (primarily corticosteroids and immunosuppressants) are used to control the disease and prevent recurrence of symptoms (known as flares). Depending on the dosage, people who require steroids may develop Cushing's syndrome, side-effects of which may include obesity, puffy round face, diabetes mellitus, large appetite, difficulty sleeping and osteoporosis. Those side-effects can subside if and when the large initial dosage is reduced, but long-term use of even low doses can cause elevated blood pressure and cataracts. Numerous new immunosuppressive drugs are being actively tested for SLE. Rather than suppressing the immune system nonspecifically, as corticosteroids do, they target the responses of individual [types of] immune cells. Some of these drugs are already FDA-approved for treatment of rheumatoid arthritis.[42]

27. Analgesia

Since a large percentage of people with SLE suffer from varying amounts of chronic pain, stronger prescription analgesics (pain killers) may be used if over-the-counter drugs

(mainly nonsteroidal anti-inflammatory drugs) do not provide effective relief. Potent NSAIDs such as indomethacin and diclofenac are relatively contraindicated for patients with SLE because they increase the risk of kidney failure and heart failure.[42] Moderate pain is typically treated with mild prescription opiates such as dextropropoxyphene and co-codamol. Moderate to severe chronic pain is treated with stronger opioids, such as hydrocodone or longer-acting continuous-release opioids, such as oxycodone, MS Contin, or methadone. The fentanyl duragesic transdermal patch is also a widely-used treatment option for the chronic pain caused by complications because of its long-acting timed release and ease of use. When opioids are used for prolonged periods, drug tolerance, chemical dependency, and addiction may occur. Opiate addiction is not typically a concern, since the condition is not likely to ever completely disappear. Thus, lifelong treatment with opioids is fairly common for chronic pain symptoms, accompanied by periodic titration that is typical of any long-term opioid regimen.

28. Intravenous Immunoglobulins (IVIGs)

Intravenous immunoglobulins may be used to control SLE with organ involvement, or vasculitis. It is believed that they reduce antibody production or promote the clearance of immune complexes from the body, even though their mechanism of action is not well-understood. Unlike immunosuppressives and corticosteroids, IVIGs do not suppress the immune system, so there is less risk of serious infections with these drugs.

29. Lifestyle changes

Avoiding sunlight is the primary change to the lifestyle of SLE sufferers, as sunlight is known to exacerbate the disease, as is the debilitating effect of intense fatigue. These two problems can lead to patients becoming housebound for long periods of time. Drugs unrelated to SLE should be prescribed only when known not to exacerbate the disease. Occupational exposure to silica, pesticides and mercury can also make the disease worsen.[32]

30.Renal transplantation

Renal transplants are the treatment of choice for end-stage renal disease, which is one of the complications of lupus nephritis, but the recurrence of the full disease is common in up to 30% of patients.[43]

31. Hughes syndrome

Hughes syndrome, also known as the antiphospholipid syndrome or sticky blood syndrome, is also related to the onset of neural lupus symptoms in the brain. In this form of the disease the cause is very different from lupus: thromboses (blood clots or "sticky blood") form in blood vessels, which prove to be fatal if they move within the blood stream.[44] If the thromboses migrate to the brain, they can potentially cause a stroke by blocking the blood supply to the brain. If this disorder is suspected in patients, brain scans are usually required for early detection. These scans can show localized areas of the

brain where blood supply has not been adequate. The treatment plan for these patients requires thinning of the blood. Often, aspirin is prescribed for this purpose, although in more severe cases anticoagulants such as warfarin are used.[5]

32. Management of pregnancy

While most infants born to mothers who have SLE are healthy, pregnant mothers with SLE should remain under medical care until delivery. Neonatal lupus is rare, but identification of mothers at highest risk for complications allows for prompt treatment before or after birth. In addition, SLE can flare up during pregnancy, and proper treatment can maintain the health of the mother longer. Women pregnant and known to have anti-Ro (SSA) or anti-La antibodies (SSB) often have echocardiograms during the 16th and 30th weeks of pregnancy to monitor the health of the heart and surrounding vasculature. Contraception and other reliable forms of pregnancy prevention is routinely advised for women with SLE, since getting pregnant during active disease was found to be harmful. Lupus nephritis was the most common manifestation.

33. Current Research in field of Lupus

Since lupus is considered to be currently incurable, current research is being geared towards finding a possible cause, a cure, and more effective treatment plans to extend and increase the quality of life for lupus patients. Several papers discuss the importance of the presence of antibodies in the brain that are only produced in patients with lupus. One such paper highlights the inhibition of astrocyte proliferation in brain tissue from lupus patient serum.[45] Astrocytes are glial cells in the brain that participate in the support of cells that form the blood brain barrier. They are extremely useful in that they provide a nutritional balance between ions in the brain, keeping it at a normal level.[46] In this study, researchers used immunofluorescence to track the antibodies near the corpus callosum to determine whether anticardiolipin antibodies have an inhibitory effect on brain cells and whether they elicit thrombus formation in brain vessels, which plays a part in neuropsychiatric lupus.

However, the majority of the recent papers focus on the effect of lupus on blood-brain barrier integrity. It was found that 20–70% of lupus patients with neurological symptoms have some form of a central nervous system involvement.[47] This can be determined using various imaging methods as well as lumbar puncture (spinal tap) to assess cerebrospinal fluid. In a study conducted in London, researchers measured the albumin content in the brain using imaging and spinal fluid. The images were used to illustrate blood brain barrier damage while the spinal tap was used to measure the protein content in the brain. Albumin is a protein that can be carried into the brain through the blood brain barrier by other transport proteins. If the ratio of albumin outside the barrier to inside the barrier is high, this means that either the barrier is damaged, or the transport proteins are not functioning well. This blood brain barrier damage can impact lupus patients by increasing their discomfort and increasing the intensity of the disease.[48]

A study called BLISS-76 tested the drug, Belimumab (HGS1006, LymphoStat-B), a fully human monoclonal anti-BLyS antibody. BLyS stimulates and extends the life of B lymphocytes, which produce antibodies against foreign and self cells. The drug, branded Benlysta, was approved by the FDA in March 2011. Notwithstanding the approval, the FDA emphasized that the drug will not work in all cases, and that more research and advanced therapies are called for. At Stanford School of Medicine Institute for Immunity Transplantation and Infection, trials are underway for use of DHEA as a therapeutic agent for the treatment of mild to moderate SLE.[49[50]. So it is clear that there is a lot of work is to be done in the field of SLE so that this auto immune disease can get a proper cure

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