Abstract

Systemic lupus erythematosus or SLE is a persistent heterogeneous autoimmune disease that affects multisystem of the body. It is distinguished by acute and chronic inflammation of various tissues and even organs of the body principally the skin and joints. Systemic lupus erythematosus is a multisystem disorder and hence, it can affect any tissues, organs and even systems of the body. There are few categories of lupus for instance, lupus dermatitis or cutaneous lupus erythematosus (CLE) that affects the skin and causes malar rash, discoid lupus erythematosus (DLE) as well as systemic lupus erythematosus that causes damage to single or multiple internal organs. The damage is due to the inflammation that is caused by direct antibody reaction to the body tissues as well the deposition of immune complexes. Glucocorticoids, immunosuppressant, and antimalarial are the combination therapy used to treat SLE besides providing counseling and awareness. Lupus erythematosus in any form particularly systemic lupus erythematosus (SLE) are prevalent in women compared to men with ratio of 6:1. It has the tendency to affect all ages but most frequently attacks women of aged 20 to 45 years old compared to men. On the other hand, if lupus erythematosus causes damage to internal organs either single or multiple, it is known as systemic lupus erythematosus. The damage is due to the inflammation that is caused by direct antibody reaction to the body tissues as well the deposition of immune complexes.

Keywords: SLE; Lupus Erythematosus; Autoimmune Disorder

Introduction

Systemic lupus erythematosus or SLE is a persistent heterogeneous autoimmune disease that affects multisystem of the body. Autoimmune disorder by definition is disease manifesting from the immune response against self-antigens. The immune system is a network of cells, tissues, and organs that work together with soluble humoral components (production of antibody against an infection) for instance, antibodies or complement to protect the body against attacks by foreign invaders. Immune system of the body has the ability to distinguish between self and foreign (microbial) agents. If these mechanisms fail in the case of autoimmune disorders, the immune system will attack the individual’s own cells and tissues by production of autoantibodies with protean clinical manifestation. In the case of systemic lupus erythematosus, the body is unable to produce normal antibodies against any infection. Instead, the body will start...
producing abnormal antibodies that is unable to recognize self and foreign microbial agents. These abnormal antibodies recognize self-antigens as foreign and consequently, it will bind and attack the self-antigens rather than foreign infectious agents. These abnormal antibodies are known as autoantibodies [1]. These autoantibodies are directed against intracellular targets. The typical types of autoantibodies that are present in at least 95% of individuals with SLE are antinuclear antibodies (ANAs). Others for instance, Anti-double-stranded DNA (dsDNA), anti-smith (anti-Sm), anti-Ro, and anti-La antibodies are rare [2]. The heterogeneity systemic lupus erythematosus is a multisystem disorder and hence, it can affect any tissues, organs and even systems of the body. For instance, when it affects the skin and causes butterfly rash, it is known as lupus dermatitis or cutaneous lupus erythematosus (CLE). Discoid lupus erythematosus (DLE) is a form of cutaneous lupus erythematosus [3].

Etiology

Specific genetic mutation such as inborn deficit of C1q, C2, and C4, as well as several polymorphisms for instance, interferon regulatory factor 5 and protein tyrosine phosphatase N22 and familial clustering of SLE or other autoimmune disease have contributed to genetic susceptibility to SLE. In addition, certain human leukocyte antigen (HLA) types including HLA-B8, HLA-DR2, and HLA-DR3 are most commonly present in patients suffering from SLE [4]. Also, defect in complement tends to have the highest risk of SLE disease, and mutations in TREX1 point to impaired regulation of endogenous nucleic acids as well contributes to the genetic predisposition to SLE [5]. Moreover, multiple genetic linkages including 1q23, 2q35.37, 6p21.11, and 12q24 suggest close relation with SLE [6]. Environmental exposures such as ultraviolet light exposure and certain viral infections for instance, Epstein-Barr virus may partake a role in susceptible individuals [2].

Pathogenesis

The definite pathogenesis of systemic lupus erythematosus still remains vague. Genetic triggers, environmental triggers, autoantibodies as well as immune complexes and complement have been identified to cause the interference in innate and adaptive immune regulatory mechanism. Intercession in the immune regulatory mechanism will further results in the interruption in apoptotic cell clearance, cytokines, B-cell immunity, and T-cell signaling that will progress in SLE pathogenesis. In general, the apoptotic cells will initiate signals like cell-surface protein such as phosphatidylinerine that will trigger the immune cells as well as macrophages and dendritic cells to phagocyte the excessive apoptotic debris. SLE is strongly associated with defects in the apoptotic clearance. Inability to remove the apoptotic remnants effectively causes the antigen presenting cells (APC) to arrest the fragments of the nuclear particles that will further cause them to interface with T & B cells. Impairment of immune regulatory mechanism further leads to increase in antigenic load and overproduction and overactive of T cells as well as the defect in suppression of B cell activation by the immune cells [8]. Further interaction will eventually leads to the development of the antinuclear antibodies which is the hallmark of this disease. Production of autoantibodies will release the immune complexes that will lead to inflammation, tissue injury and cell and organ damage that will progress in SLE disease. Genetic factors for instance, polymorphisms in components of the toll-like receptor (TLR) that usually increases the production of type 1 interferon as well as interferon regulatory factor 5 and protein tyrosine phosphatase N22 and familial clustering of SLE have been identified to contribute to the genetic susceptibility to SLE. In addition, major histocompatibility complex (MHC) class II alleles with human leukocyte antigen (HLA) types including HLA-B8, HLA-DR2, and HLA-DR3 are most commonly associated with SLE [5].

Statistics of Systemic Lupus Erythematosus in Malaysia

Lupus erythematosus in any form particularly systemic lupus erythematosus (SLE) are prevalent in women compared to men with ratio of 6:1 [9]. About 90% cases reported out of SLE are women while the other 10% are men and children. It has the tendency to affect all ages but most frequently it attacks women of aged 20 to 45 years old compared to men. In Malaysia, it has been estimated that more than 10,000 people have been diagnosed from SLE over the past 30 years but this count is only at the tip of the iceberg [10]. There are many people who are suffering from SLE that have not been diagnosed according to the Malaysian SLE Association as they did not approach the doctor for consultation.

Signs and symptoms

In general, patients who suffer from systemic lupus erythematosus usually come over with complaints of general symptoms such as fatigue, weight loss, fever as well as myalgia and arthralgia [11]. Fatigue is the commonest symptom that patients often complain about that can actually make them enfeeble. The hallmark symptom of this disease is red, butterfly rash on the skin particularly on the cheeks. In terms of dermatology, there are three types of lesions which are Acute Cutaneous Lupus, Sub-Acute Cutaneous Lupus and Chronic Cutaneous Lupus. Cases have been reported that up to 61.3 % of SLE patients suffer from red, butterfly rash on the cheeks sparing the nasolabial folds and the degree of intensity may vary [12]. Also, red plaques without scarring may develop on the skin area that is exposed to the Sun and
it is known as acute cutaneous lupus. Non-scarring and soft
skin lesions that are often intermittent are known as sub-acute
cutaneous lupus. On the other hand, in discoid lesions
or chronic cutaneous lupus, red plaques may be accompanied
by alopecia which is loss of hair at particular area where
the red plaques are developed [9]. Besides, oral and nasal ulcers
may also manifest in 51% of SLE patients and usually are
quite painful [12]. Besides, musculoskeletal system is the
commonest system that affects most of the patients who are
diagnosed from systemic lupus erythematosus. The typical
symptoms that patients usually present with are arthritis and
arthralgia that usually affects the small joints of the hands,
wrist as well as the knees [3]. In some cases, patients have
come up with symptoms of dysphagia, heartburn, abdominal
pain, as well as vasculitis. Clinical pericarditis and pleuritis
have been reported up to 63% of the autopsy cases [1,13,14].

Diagnosis

According to 2012 SLICC Criteria, an individual is being
diagnosed suffering from SLE if the biopsy revealed nephritis
with ANA or antidsDNA antibodies or he/she fulfill four of
the clinical criteria with at least one clinical criteria and at
least one immunological criteria. Clinical criteria includes
acute or chronic cutaneous lupus, oral or nasal ulcers, non-
scarring alopecia, synovitis, serositis with pericardial
more than 24 hours, renal of which > 500 mg proteinuria/24 hours
or RBC casts, neurologic symptoms which includes seizures,
psychois, mononeuritis multiplex, myelitis, peripheral or
cranial neuropathy or acute confusional state, hemolytic
anemia, lymphopenia or thrombocytopenia [6]. In terms of
immunological criteria, individual who are diagnosed to be
suffering from SLE shows at least one positive result for ANA
or antidsDNA or antiSmith or antiphospholipid antibodies
or Direct Coombs test in the absence of hemolytic anemia
[3]. Direct immunofluorescence also being carried out and
the typical finding includes antibody deposition which are
typically granular and composed of IgG or IgM or sometimes
might be IgA as well at the dermal–epidermal junction and
around hair follicles [9].

Treatment

To treat SLE completely is impossible and onerous as it
causes relapse. Thus, the ultimate goal of SLE treatment is
to stop the organ inflammation, avert the irreversible organ
damage as well as to suppress the immune response causing
the inflammation and flares and to lower down the intensity of
pain. The drugs that are used to treat SLE are glucocorticoids
and the target dose of glucocorticoids should be 0.25 mg/
k/kg every other day for 2 to 3 months [15]. Patients who are
under chronic steroid therapy should be evaluated closely as
they are prone for fever or any infection. Next, antimalarial
drugs such as hydroxychloroquine and chloroquine are
prescribed for skin and mucocutaneous manifestations [16].
Study has been done and proven that the use of antimalarial
drugs has resulted in greater than 50% reduction of SLE manifestation. Immunosuppressive drugs like azathioprine,
methotrexate or cyclophosphamide are given to the patients
who are suffering from severe renal or cerebral disease at
which the other therapies have failed or for those who are
unable to tolerate with corticosteroids [17].

Discussion

The outcome of this study reveals the latest usage of
rituximab as the drug of choice in the treatment of SLE.
In the randomized controlled trials, it has shown some
improvement in the prognosis of SLE but the usage of Rituximab reveals negative results in terms of renal and
non-renal [6]. The clinical research of this drug has not been
thoroughly tested yet and further study and trials need to be
done to improvise so there will be less adverse reaction and
better prognosis as the outcome for renal was negative. If this
drug is possible to treat the patients in terms of renal, it would
be a great discovery to save most of the SLE patients who
ended up of having end stage kidney disease. On the other
hand, in March 2011, the US Food and Drug Administration
have given the green light for the usage of Belimumab as a
part of the treatment of SLE in the adults [9]. It has good
prognosis in terms of reducing the time to develop flares
and lower the exposure towards glucocorticoids. Based on
the latest study, we found that the five year survival rate has
improved in more than 90% of SLE patients with the usage of
imunosuppressant therapy [6]. However, most of the
patients develop relapse and their condition deteriorate and
this worsen in SLE patients with lupus nephritis [18-20].

Conclusion

The mortality rate of patients who suffer from SLE is
thrice higher than the general populations. Studies and results
obtained highlight the desideratum for further research and
clinical progress. More research needs to be done together
with clinical trials to improve the prognosis and the quality
of life of patients who suffers from SLE. Vigilant follow up,
inventing latest most effective drugs as well as improving the
diagnostic research methods will one day prove that SLE can
be treated with complete convalescence.

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