

LIFE THREATENING COMPLICATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS- AN OVER VIEW

PR. Roshni*, Sreya Pushpan, Devu Pavithran and Kevin Krepash

Department of Pharmacy Practice, Amrita School of pharmacy,
Amrita Vishwavidhyapeetham University,
AIMS Health Science Campus, Kochi, Kerala, Thiruvanthapuram, India.

ABSTRACT

SLE has wide range of symptoms. These symptoms can develop slowly and appear suddenly. Many patients with SLE have "flares," in which symptoms suddenly worsen and then settle down for long periods of time. The primary cause of death in lupus is atherosclerosis leading to cardiovascular disease. Multiple organs including skin (necrosis), hematologic (thrombocytopenia, haemolytic anaemia, neutropenia, catastrophic anti phospholipid syndrome and thrombotic thrombocytopenia purpura), heart (pericardial tamponade, myocarditis), lung (alveolar haemorrhage, pulmonary hypertension), gastrointestinal (vacuities, pancreatitis), adrenal insufficiency, neurologic (myelitis) are encountered.

Keywords: SLE, lupus, complications, disease.

INTRODUCTION

SLE or lupus is a systemic auto immune disease that can affect any part of the body. Like in any other auto immune diseases, the immune system attacks the body's cells and tissues, resulting in inflammation and tissue damage¹. It is a both type II and type III hyper sensitivity reaction in which bound Antibody-Antigen pairs precipitate and cause a further immune response.

SLE mainly causes damage to the Heart, Joints, Lungs, Blood vessels, Liver, Kidney and the Nervous system. Studies showed that about 80-90% of the total patients reported to have SLE were females^{2,3}.

Since SLE is a heterogeneous disease complications may vary from person to person. The intensity or severity of the complications mainly depends on the area affected starting from skin to various internal organs.

Thrombocytopenia, haemolytic anemia, neutropenia, leukopenia, blood cancer, catastrophic antiphospholipid syndrome, and thrombotic thrombocytopenic purpura, atherosclerosis, pericardial tamponade,

myocarditis, heart failure, alveolar haemorrhage, pulmonary hypertension, vasculitis, pancreatitis, adrenal insufficiency, lupus nephritis, psychiatric or neurologic disorders, arthritis and myelitis are some of the major complications of SLE.

Complications

Complications of Blood

Thrombocytopenia

In case of thrombocytopenia the antibodies attacks the blood platelets which may cause their destruction. This in turn may lead to impaired blood clotting which is often manifested as bruising and bleeding from the skin, nose, intestine etc.

Chronic thrombocytopenia can be treated by using methyl prednisolone (1000mg daily for 3 days, given over 90min.) which is followed by high dose of oral prednisolone. IV immunoglobulin 400mg/kg over 5 days is given to patients who do not respond. If either therapy is found ineffective then Rituximab therapy is initiated. In addition to this

Mycophenolate and Azathioprine may be given as maintenance therapy⁴.

Haemolytic Anaemia

The major cause of haemolytic anaemia is high levels of anticardiolipin antibody. It is very rare in SLE. Direct coomb's test, high LDH, high reticulocyte count are some of the diagnostic tests used to detect haemolytic anaemia.

Haemolytic anaemia can be treated by using methyl prednisolone (1000mg daily for 3 days, given over 90min.) which is followed by high dose of oral prednisolone (1mg/kg). In addition to this Mycophenolate and Azathioprine may be given as maintenance therapy⁴. Danzol is also used⁵. In refractory haemolytic anaemia Rituximabtherapy^{6,7} or splenectomy⁸ is done.

Leukopenia and Neutropenia

Leukopenia is one of the most common complications of SLE and the most common among them is Lymphopenia. Where as in other hand neutropenia is rare in SLE, but it was reported^{9,10}.

Drugs like Rituximab are found to induce neutropenia. Presence of antineutrophil antibodies and drug toxicity to certain drugs like cyclophosphamides or immunosuppressant may be an indication of neutropenia.

Blood Cancer

Since SLE and other autoimmune diseases tend to affect lymph nodes, they may lead to Hodgkin's and Non Hodgkin's lymphoma.

Catastrophic Antiphospholipid Syndrome (CAPS)

CAPS is a rare manifestation of APS. About 34-42% of patients with SLE are presented with APS. It is often marked by the presence of anticardiolipin and lupus anticoagulant. APS may ultimately lead to deep vein thrombosis.

The main three goals of treatment are to decrease 'cytokine storm' by using IV methyl prednisolone, to treat thrombosis by using IV heparin and to decrease anti phospholipid antibody syndrome by using by using IV immunoglobulin¹¹.

Thrombotic Thrombocytopenic Purpura

Patients with TTP are also found to have CAPS^{12,13}. Fever, thrombocytopenia, microangiopathic haemolytic anaemia, renal dysfunction and neurological dysfunction are included in the thrombotic thrombocytopenic purpura¹⁴.

Evaluation includes peripheral blood smear for schistocytes, exclusion of infection and drug toxicity.

Plasma exchange/ plasmapheresis are the main treatment in TTP¹⁵. Also IV cyclophosphamide and rituximab are also given^{16,17}.

Complications of Heart

Atherosclerosis

The main cause of death in lupus is atherosclerosis which lead to cardiovascular disease. This is the chronic inflammation associated with SLE which cause formation plaques inside the heart arteries which lead to coronary heart disease or heart attack.

SLE treatments drugs like corticosteroids can affect the cholesterol, weight and other factors that harm the heart.

Pericardial Tamponade

Pericarditis is mainly seen in SLE but pericardial tamponade is rare. It occurs as the clinical manifestation of SLE¹⁸. In Pericarditis patient feels dyspneic lying flat and feels better leaning forward. Patient with tamponade are present with ascites and edema¹⁹.

Myocarditis

Only 14% of the people are affected by myocarditis, it is very rare²⁰. It may be associated with myositis²¹. It is evaluated by electrocardiogram which rule out hypokinesia and coronary arteriogram which will show atherosclerosis and coronary vasculitis. In some instances right ventricular biopsy also confirms myocarditis²².

Treatment includes IV methyl prednisolone and also high dose oral prednisolone (1mg/kg).²³ Cyclophosphamide therapy is also done.²⁴

Complications of Lung

Alveolar Haemorrhage

Alveolar haemorrhage is very rare in SLE, only few cases are there.²⁵⁻²⁷ Dyspnea, fever, hemoptysis and chest pain are present with this. Chest CT and bronchoscopy are used to diagnosis alveolar haemorrhage.

Treatment include plasmapheresis and IV methyl prednisolone (1000mg daily for 3 days, given over 90min) followed by oral prednisolone (1mg/kg).

Pulmonary Hypertension

Pulmonary hypertension can be severe in SLE with poor prognosis.²⁸ Dyspnea is the most common symptom. Evaluation includes ECG followed by right heart catheterization.

Treatment requires surgical embolectomy or thrombolytic agent or heparin. It is treated with IV methyl prednisolone and followed by oral prednisolone. Chronic pulmonary hypertension can be treated as that of idiopathic pulmonary hypertension which includes sildenafil, bosentan, and IV prostacyclin.²⁹

Complications of GI

Pancreatitis

Only 4% of people with SLE has this complication.³⁰ It can be fatal for paediatric patients.³¹ The history of pancreatitis include hypertriglyceridemia, psychosis, pleurisy, gastritis and anaemia.³⁰ High dose of corticosteroids can cause pancreatitis. Treatment includes IV methyl prednisolone for 3 days.

Vasculitis

In vasculitis patient may present with fever, abdominal pain, diarrhoea, vomiting and sepsis^{32,33}. The differential diagnosis include atherosclerosis, peptic ulcer, peritonitis, bowel infarction and infections like *C.difficile* or cytomegalovirus.

Treatment includes surgical dissection or suppression of vasculitis by IV methyl prednisolone.

Adrenal Insufficiency

It usually present with flank pain, nausea, vomiting, hypotension and electrolyte abnormalities. Treatment of acute adrenal insufficiency done with steroids and chronic has done with adrenal replacement with low dose prednisolone and fluorinated steroids.

Complications of Skin

Cutaneous Digital Gangrene

Cutaneous digital gangrene will start as small ischemic lesions but quickly develop to digital gangrene. In long term disease Raynaud's phenomenon and elevated serum CRP were independent risk factors. The diagnosis includes severe Raynaud's phenomenon thromboembolic (i.e. antiphospholipid syndrome [APS]) and lupus vasculitis. Elevation requires the assessment of anti phospholipid antibodies (lupus anticoagulant, anticardiolipin)

Treatment includes for Reynaud's syndrome calcium channel blockers are given and also topical nitrates. For thrombosis low dose aspirin (81mg) and therapeutic dose of heparin is given. For vasculitis methyl prednisolone followed by oral prednisolone is given. The main goal is to save ischemic tissue as possible.

Cutaneous Necrosis

Necrosis can form by antiphospholipid syndrome. It can be induced by warfarin and also in patient deficient with protein c. Evaluation include assessment of antiphospholipid antibody and biopsy at the edge of necrotic area. Heparin is given if necrosis is due to APS and IV methylprednisolone followed by oral prednisolone if necrosis is due to SLE vasculitis.

Complications of Kidney

Lupus Nephritis

Lupus nephritis is the condition in which the inflammation of kidney. It is common in SLE. In early stages lupus nephritis can cause fluid build up leading to swelling in extremities like feet, legs, hands, arms and overall weight gain. Untreated nephritis may lead to complete renal failure.

The evaluation of lupus nephritis is mainly by kidney biopsy and thus classifying the severity condition. Patient with lupus nephritis should maintain their BP 130/80 mmHg or below.

Treatment of lupus nephritis mainly includes Hydroxychloroquine. Severe to moderate lupus nephritis is mainly treated with immunosuppressants like cyclophosphamide or mycophenolatemofetil. But for mild or very severe lupus nephritis immunosuppressant is not recommended.

Complications of CNS

Myelitis

This may occur as two types one is affecting grey matter and other affecting white matter. Pain, weakness and sphincteric defects are the main symptoms of myelitis.³⁴ Spasticity and hyperreflexia are the main dysfunctions of patients that affecting white matter and flaccidity hyporeflexia are the dysfunctions of patients that affecting grey matter.

Treatment should be given short time after onset of symptom. IV methyl prednisolone (1000mg daily for 3 days, given over 90min), followed by high dose oral corticosteroids. Rituximab can also be given.

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