



Systemic Lupus Erythematosus: A case series and review

Dr Rutuja Kibe

Medical Officer, Ministry of Health, Pune;

Dr Nishit Biniwale

Physician, Biniwale Clinic, Pune;

Dr Atul Biniwale

Physician, Biniwale Clinic, Pune

ABSTRACT

Systemic Lupus Erythematosus(SLE), also known as lupus, is a chronic multisystem autoimmune inflammatory disease. It affects young females 10 times more than males. SLE can affect every organ in the body. Common manifestations include rash, arthritis and fatigue. At the more severe end of the spectrum, SLE can cause nephritis, neurological problems, anemia and thrombocytopenia. SLE is a relapsing and remitting disease, and treatment aims are threefold: managing acute life-threatening episodes, preventing flare ups during disease remissions, and controlling the incapacitating day to day symptoms. Serology and tissue biopsy play a key role in establishing diagnosis before treatment is initiated. Hydroxychloroquine and non-steroidal anti-inflammatory drugs are used for milder disease; corticosteroids and immunosuppressive therapies are generally reserved for major organ involvement; anti-CD20 monoclonal antibody is now used in patients with severe disease who have not responded to conventional treatment. Despite enormous improvements in prognosis since the introduction of corticosteroids and immunosuppressive drugs, SLE continues to have a significant impact on the mortality and morbidity of those affected.

KEYWORDS

SLE, vasculitis, autoimmune, lupus, nephritis

INTRODUCTION

SLE is a clinically heterogeneous disease that has been described by Hippocrates in 375 BC. It is autoimmune in origin, and characterized by the presence of autoantibodies directed against nuclear antigens. It can affect any organ system, but it mainly involves the skin, joints, kidneys, blood cells, and nervous system. It usually follows a remitting and relapsing course, with the first manifestations frequently starting at childbearing age. Here we present a series of SLE cases that had different modes of presentation and we briefly review the disease entity and the latest management guidelines. It is notable that three patients in our series conceived successfully, had uneventful term pregnancies and gave birth to healthy children

CASE 1:

A twenty-year-old woman developed chronic progressive pain and swelling involving the small joints of the hand. She had been having these complaints for two years, during which she had a first trimester pregnancy loss. Recently she also had intermittent low grade fevers, weight loss and breathlessness. On admission, her chest x-ray showed a pleural effusion which on tapping demonstrated exudative characteristics. The following day she complained of weakness in her limbs. Examination showed a lower motor neuron, flaccid quadriplegia (Power grade 2) with areflexia and sensory loss. NCV studies showed a BL diffuse severe sensory-motor neuropathy affecting all four extremities. She was diagnosed with SLE on clinical grounds and by biochemical evidence - a positive ANA and dsDNA titres. Her hemoglobin levels were 5.7 gm%, ESR was 70mm/hr. and her urinalysis demonstrated proteinuria and hematuria. She was started on pulsed prednisolone, transfused blood and given a dose of cyclophosphamide. Her disease was kept quiescent for two years after which she had another pregnancy which was successfully carried till term. She was kept on alternate day low dose oral steroids which ensured the pregnancy remained uneventful. Post-delivery her ESR was closely monitored and she was maintained on azathioprine (AZA). Since then she has had infrequent relapses of the disease which were treated with cyclophosphamide and intravenous steroids.

CASE 2:

An eighteen-year-old female engineering student developed bilateral pedal swelling and mild facial puffiness which seemed to be progressing for a few weeks. On examination, a red

maculopapular rash was evident over her cheeks and nasal bridge. A urine routine demonstrated 4+ proteinuria which was quantified as 3gms on 24hr sampling. Her ESR and CRP were 70 mm/hr. and 120 mg/L respectively. An ANA, dsDNA and later a renal biopsy confirmed the diagnosis of SLE. Mesangioproliferative changes with few crescents were noted on the biopsy and both C3 and C4 levels were low. She was given pulsed doses of prednisolone and cyclophosphamide which were later replaced with azathioprine and hydroxychloroquine. On follow up her urinary protein was 1 gm at 6 weeks which improved further to 400 mg at 6 months with normalization of ESR. She was subsequently lost to follow up in which time she conceived though it had to be terminated as her renal disease worsened considerably with development of pancytopenia. AZA was added to her treatment regimen and the disease remained quiescent for 2 years. Under the cover of low dose steroids and AZA the patient became pregnant. The pregnancy and delivery were both uneventful. She developed secondary hyperparathyroidism and anemia which were treated with vitamin D and erythropoietin respectively. She is maintained on alternate day low dose of steroids and AZA.

CASE 3:

A twenty-one-year-old female was referred to the clinic for having two spontaneous second trimester pregnancy losses. In the process of being investigated she also developed complaints of patchy hair loss and a malar rash. Tests for ANA and dsDNA came back positive; her urine routine showed a slight proteinuria of 500 mg; ESR and CRP were elevated. She was diagnosed as a case of SLE further confirmed by a skin biopsy of the rash. She was started on prednisolone which led to a quick remission and the dose was tapered. Subsequently she conceived and had an uneventful pregnancy and delivery. Her SLE went into remission and her medications were stopped. She had another successful pregnancy 2 years later. After a year, she needed to be hospitalized because her hemoglobin dropped to 4 gm/dl; a 3+ proteinuria with urea and creatinine elevations were documented. This relapse was possibly attributed to uro-sepsis, which preceded the event. Immediate treatment with 6 weekly pulsed methylprednisolone was initiated and continued for three years. She was also given AZA. Eventually her proteinuria resolved however creatinine remains elevated at a level of about 2 mg/dl till today. Currently she is only on AZA.

CASE 4:

A twenty-four-old female presented to the clinic with a two-month history of excessive fatigue and breathlessness. On examination, she was pale and a malar rash was noted. Investigations revealed pancytopenia with a hemoglobin of 5 gm%, WBC of 2800, platelets of 85,000; elevated LDH, ESR and CRP. She was transfused and was concurrently started on Iron and B12 supplementation as the anemia was dimorphic. A bone marrow biopsy was done which revealed a hypo-cellular marrow. She tested positive for ANA, dsDNA; her C3 and C4 levels were low. She was diagnosed as a case of SLE which was confirmed by a skin biopsy of the rash. Treatment was initiated with blood transfusions, pulse methylprednisolone and cyclophosphamide. She responded well and was later maintained on Prednisolone and AZA.

DISCUSSION:

SLE is a multisystem, autoimmune disease, involving complex pathogenetic mechanisms that can present at any age, though it is commonly seen in women in the reproductive age group¹. The disease is prone to relapses and remissions, resulting in considerable morbidity² due to flares of disease activity and accumulated damage³. The disease can present with slowly or rapidly progressive active disease at any age and can be associated with the rapid accumulation of damage if not promptly diagnosed, appropriately treated and regularly monitored⁴. SLE diagnosis still represents a challenge, remaining largely based on a clinical judgment. It is important to ensure that the diagnosis of lupus is appropriate before considering treatment⁵ given the variety of clinical manifestations that can occur, lupus should be considered in the differential diagnosis of many acute and sub-acute presentations⁶. The clinical and laboratory criteria for diagnosis have been defined by the American College of Rheumatology which are 85% sensitive and 95% specific⁷.

The presence of anti-dsDNA antibodies, low complement levels or anti-Smith (Sm) antibodies and LE cells are highly predictive of a diagnosis of SLE in patients with relevant clinical features. ANA are present in about 95% of patients and although sensitive are not specific for the diagnosis of lupus. Antiphospholipid antibodies should be tested in all lupus patients at baseline, especially in those with an adverse pregnancy history (e.g. recurrent fetal loss or any unexplained fetal death after 10 weeks' gestation) as was with one of our patients⁸. C3 and C4 levels are useful as falling, low complement levels are associated with flare⁹ particularly in patients with lupus nephritis¹⁰ which is one of the most serious manifestations of SLE. Proteinuria should be quantified using urine protein:creatinine ratio or 24-hour urine collection¹¹. Erythrocyte sedimentation rate (ESR) is often raised in active SLE¹². Anti-Ro and La antibodies are associated with neonatal lupus (including congenital heart block) and should be checked prior to pregnancy.

It is important to monitor lupus patients regularly to assess and monitor changes in disease activity, chronic damage, drug-induced and co-morbid conditions that may be confused with lupus and that are associated with an increased risk of death. Steroids can be used in mild/moderate disease or flare ups in the form of oral and pulsed doses respectively¹⁴. AZA treatment has been associated with prevention of flares and a reduction in corticosteroid dosage and for maintenance therapy after remission. It suitable for long term therapy particularly in women desiring pregnancy¹⁵, pregnant or breast-feeding women¹⁶. The efficacy and safety profile of hydroxychloroquine is good and although it can cross the placenta, exposure is not associated with significant adverse effects on the fetus¹⁷. IV Cyclophosphamide is used to reduce disease activity and corticosteroid usage in severe lupus, both in renal and non-renal involvement¹⁸.

Hydroxychloroquine has anti-thrombotic as well as anti-inflammatory properties and by reducing disease activity in the mother may improve the outcome of the child by improving placental function¹⁹. Additional monitoring investigations should include Vitamin D3 which is often low, because of sun avoidance and/or chronic kidney disease. Vitamin D is required for optimal bone health especially in patients on chronic glucocorticoid

therapy and/or following the menopause²⁰. Lupus patients should be advised about avoidance of sun and other sources of UV irradiation and the use of sunscreens should be promoted.

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