INTRODUCTION

Systemic lupus erythematosus is considered as “the great mimic of other conditions”. Conversely there are many diseases which can mimic SLE as a systemic disease or as dermatological, rheumatological, vasculitic, or immunological mimickers. This monograph is restricted to the lupus mimickers only, not the discussion on SLE.

DERMATOLOGICAL MIMICKERS OF S.L.E. 1,2

I. Dermatological conditions mimicking acute cutaneous lupus erythematosus (LE)

Rosacea: Rosacea is characterized by erythema of the central face that has persisted for months or more. The convex areas of the nose, cheeks, chin, and forehead are the characteristic distribution [Fig. 1]. Triggers of rosacea may include hot or cold temperature, sunlight (hence, photosensitive), wind, hot drinks, spicy foods, exercise, emotions, alcohol, cosmetics, topical irritants, menopausal flushing, medications etc. Erythematotelangiectatic subtype and papulopustular subtype may mimic acute cutaneous LE. The malar erythema of lupus erythematosus [Fig. 2] can be difficult to differentiate from rosacea3. The presence of pustules and papules or blepharitis favors a diagnosis of rosacea, while fine scaling, pigment change, follicular plugging and scarring favor a diagnosis of lupus. In occasional patients, histologic examination of involved skin may be necessary for distinction.

Seborrheic dermatitis: Seborrheic dermatitis of the face may closely mimic both early rosacea and the butterfly lesions of systemic lupus erythematosus4. In contrast to seborrheic dermatitis, lupus erythematosus rarely affects the nasolabial folds and often has a clearly demonstrable photodistribution.

Chloasma / Melasma: It is combined epidermal and dermal hyperpigmentation of forehead, cheeks, and perioral area. It is a common problem, almost exclusively limited to women; extremely prevalent in Latin America, among patients with mixed Indian/Spanish background. Risk factors include sun exposure, pregnancy or use of oral contraceptives. This photosensitivity reactions and distribution over the face...
Fig. 2: Facial rash of Systemic Lupus Erythematosus may mimic acute cutaneous LE.

II. Dermatological conditions mimicking sub-acute cutaneous LE

The lesions of sub-acute cutaneous lupus erythematosus (SCLE), when predominantly papulosquamous in appearance, may be similar to the appearance of photosensitive eczema or psoriasis. Dermatophytosis, granuloma annulare, erythema annulare centrifugum or other annular erythemas may simulate SCLE, when the lesions are predominantly annular.

III. Dermatological conditions mimicking chronic cutaneous LE or discoid LE

Polymorphous light eruption, lichen planus, leukemia cutis, lymphoma cutis, granuloma faciale, tinea faciei, psoriasis, lupus vulgaris and sarcoidosis mimic chronic form of cutaneous lupus, discoid lupus erythematosus (DLE). Histologic and DIF evaluation are often necessary to make a definitive diagnosis of DLE.

Polymorphous light eruption: Polymorphous light eruption (PMLE) is a common, sunlight-induced eruption affecting individuals of all races. The diagnosis of PMLE is suggested by its characteristic history, clinical findings, and lack of circulating antinuclear and other lupus erythematosus-associated antibodies. Lesions of LE tend to last for weeks to months, whereas PMLE lesions, in the absence of further sun exposure, usually resolve within days. Polymorphous light eruption may clinically simulate tumid lupus, but histologically the two can usually be distinguished.

Lichen planus (LP): The disease most difficult to differentiate from LP is LE, particularly in patients with oral or scalp lesions alone. In these patients, the diagnosis of LE may only be made after additional biopsies are performed or other signs of LE appear. Direct immune-fluorescence (DIF) studies are helpful. Some lichenoid drug eruptions have a photodistribution. The most commonly incriminated drugs include angiotensin-converting enzyme (ACE) inhibitors, thiazide diuretics, antimalarials, quinidine and gold.

Tinea faciei: This facial dermatophyte infection is characterized by erythematosus, often with scaly patches; not annular because of facial configuration; pruritic; may worsen with light exposure. It mimics DLE which is slower to develop and more persistent; has prominent follicles, may be painful.

Lupus pernio / cutaneous sarcoid: It is red-violet chronic infiltrate on tip of nose; often associated with chronic pulmonary involvement and digital bone cysts. Upon diascopy, in which pressure induces blanching, the lesions are said to have the color of ‘apple jelly’.

RHEUMATOLOGICAL AND MUSCULOSKELETAL MIMICKERS OF S.L.E.

Rheumatoid arthritis, systemic sclerosis and scleroderma, Sjogren’s syndrome, mixed connective tissue disorder, dermatomyositis, polymyositis mimic features of SLE. These connective tissue diseases are a family of closely related disorders. These diseases have a number of common features. The most common symptoms at presentation include Raynaud’s phenomenon, arthralgia, or arthritis; mucocutaneous symptoms such as photosensitivity, malar rash, alopecia, and oral ulcerations; fever sicca symptoms, or CNS symptoms.

Söjgren’s Syndrome: Söjgren’s syndrome is a chronic autoimmune disorder that can occur alone (primary Sjögren’s syndrome) or in association with other autoimmune diseases, most commonly systemic lupus erythematosus and rheumatoid arthritis (RA) [secondary Sjögren’s syndrome].

Many of the clinical and serological features of Sjögren’s syndrome and SLE make the precise diagnosis difficult because there are similarities between the two diseases.

- Those with primary Sjögren’s syndrome and those with SLE have other similar disease symptoms, including:
  - Arthritis
  - Skin rash
  - Kidney disease.
- Autoantibodies are common in Sjögren’s, with 80% testing positive for antinuclear antibodies (ANA), Rheumatoid factor in 75% to 95%.9
Lupus and Rheumatoid Arthritis

In lupus, joint pain (arthralgia) is common. Joint swelling (arthritis) may be present in some cases, but the majority of those with lupus experience joint pain without swelling or only intermittent swelling. Early rheumatoid arthritis may mimic lupus. In rheumatoid arthritis, joint swelling is always present and pain is common but less prominent. Because rheumatoid arthritis is more likely than lupus to cause joint deformities and bone destruction, joint replacement or reconstructive surgery is more often required in RA than in SLE.

Myositis

Many persons with lupus have muscle pain (myalgia), but a few have muscle weakness due to inflammation (myositis). In polymyositis-dermatomyositis (PM-DM), the primary problem is proximal muscle weakness due to muscle inflammation. Typically, there is little or no pain associated with the weakness. People with myositis have increased blood level of creatine kinase with abnormal electromyogram (EMG), associated with muscle cell degeneration with inflammation found in muscle biopsy. Characteristic pathognomonic skin rash (es) is dusky red, and may appear in malar distribution mimicking the classic SLE “butterfly rash”. Shawl sign, heliotrope rash, and Gottron’s sign seen over the dorsum of the PIP and MCP joints are highly suggestive of dermatomyositis. Presences of ANA, anti-Jo1 antibody are seen in patients with associated interstitial lung disease.

Lupus and Scleroderma

The hallmark of scleroderma (SSc) is thickened skin which affects the fingers, and often the hands, forearms, feet, and face due to the excessive production and uncontrolled laydown of collagen. Classical “salt-and-pepper” pigmentation is seen in SSc. The varieties of skin rashes seen in lupus are due to inflammation, rather than fibrosis. Other features which are less common in SLE than in SSc include: pulmonary fibrosis, difficulty in swallowing solid, and heartburn or indigestion from stomach acid “refluxing”, and deformities of hands. Raynaud’s phenomenon occurs in 95 percent of people with scleroderma and in 40 percent of persons with lupus. Anti-nuclear antibody is found to be present in both the situations; but anti-topoisomerase-1 antibody (in diffuse SSc) and anti-centromere antibody (in localized SSc) are found to be present in scleroderma.

Mixed Connective Tissue Disease (MCTD)

Some individuals have symptoms and signs of more than one connective tissue diseases, e.g., lupus, polymyositis-dermatomyositis, and scleroderma, and is known as MCTD. These persons often (but not always) have one specific blood antibody in their blood (anti-U1RNP antibody) but not the other antibodies commonly associated with SLE, SSc, or PM-DM.

VASCULITIC AND IMMUNOLOGIC MIMICKERS

This group includes primary and secondary vasculitis mimicking SLE. Secondary vasculitic disorders are composed of infectious diseases and malignant diseases. Diseases causing primary vasculitis are those described above under heading of rheumatological diseases mimicking SLE. Secondary vasculitides mimicking SLE are as follows:

Infectious Diseases

- **Viral**: Hepatitis C, hepatitis B, parvovirus B19, HIV, infectious mononucleosis (Epstein-Barr Virus)
- **Bacterial**: Lyme’s disease, disseminated gonococcal arthritis, atypical mycobacteria, syphilis (secondary)
- **Parasitic**: viscerale leishmaniasis

Malignancy: Hematological malignancies (Hodgkin’s lymphoma), thymoma; carcinoma of the lung, breast, and ovary as paraneoplastic syndromes may mimic SLE. A malignancy can cause anemia, elevated ESR, positive ANA, vasculitis, and other autoimmune phenomena mimicking SLE. An unusual case of disseminated gastric signet ring cell carcinoma was reported mimicking systemic lupus erythematosus.

Hepatitis C mimicking lupus: Chronic HCV infection does not target only the liver, but has a profound effect on the immune system and sometimes mimics SLE. Deposition of immune complexes containing cryoglobulins in different organs is the presumed disease mechanism in mixed cryoglobulinemia, characterized by purpura, arthralgias (or more rarely, arthritis), glomerulonephritis, and polyneuropathy. Unselected patients with chronic HCV infection display a number of autoantibodies including antinuclear antibodies (10%).

Parvovirus B19: Parvovirus B19, a virus which commonly runs an asymptomatic or benign self-limiting course such as erythema infectiosum, transient aplastic crisis, flu-like symptoms, rash, arthralgia, and arthritis can present with multi-systemic symptoms resembling SLE, both clinically and serologically. Similarities have been so striking that patients have been initially misdiagnosed with SLE, having fulfilled 3-5 of the criteria of the American College of Rheumatology,
currently used for the diagnosis of SLE, only to discover later that they were infected by parvovirus B19. HIV: A Sjogren’s-like syndrome, termed diffuse infiltrative lymphocytosis syndrome (DILS) is now a well-established manifestation of HIV infection that may present to the rheumatologist. The diagnosis may be missed because most of these patients do not have AIDS, and may well have a lymphocytosis rather than a lymphopaenia. Furthermore ANA in low titer and antiphospholipid antibodies may mimic SLE.

Acute Lyme arthritis: Lyme disease has been called “the new great mimicker” because its protean manifestations resemble those of other diseases. Acute Lyme arthritis can mimic other causes of monoarticular or pauciarticular arthritis, including reactive arthritis and other seronegative spondyloarthropathies, juvenile rheumatoid arthritis, and systemic lupus erythematosus.

Mycobacterium tuberculosis: One cutaneous manifestation of M. tuberculosis infection is ‘lupus vulgaris’, the nomenclature suggesting that the two diseases have historically shared similarities in their dermatological manifestations.

Visceral leishmaniasis: Visceral leishmaniasis can present with fever, splenomegaly, pancytopenia, hypergamma-globulinemia, and autoantibody (ANA) production. These features may mimic SLE, but massive firm splenomegaly, very high acute phase reactants, and activation of coagulation system with high D-dimers point toward infection.

Sarcoidosis: It is an immunological mimicker of SLE. Positive ANA is reported in association with sarcoidosis in up to 33% of patients during the acute phase, but antibodies to double-stranded DNA have not been reported. Fever, arthritis, mouth ulceration, and pleuropericarditis have all been described, both in early and in active chronic sarcoidosis, together with non-specific rashes - all mimicking SLE.

SEROLOGICAL MIMICKERS

Anti-nuclear antibody (ANA) is highly sensitive for diagnosing SLE and it is present in > 95% of cases of SLE. But, several other connective tissue disorders and non-rheumatic diseases, which show positivity to ANA, may mimic SLE. Most important condition is drug-induced lupus.

Drug-induced lupus (DIL): DIL should be suspected in patients who do not have a diagnosis or history of SLE, who develop a positive ANA and at least one clinical feature of SLE after an appropriate duration of drug exposure, and whose symptoms resolve after discontinuation of the drug. Antihistone antibodies are present in more than 95% of cases, whereas hypocomplementemia and anti-DNA antibodies are rare. A variety of drugs have been identified as being definite, probable, or possible causes of lupus - procainamide, quinidine, hydralazine, methyldopa, tumor necrosis factor-? blockers, carbamazepine, phenytoin, isoniazid, minocycline, nitrofurantoin and so many.

NEUROLOGICAL MIMICKER OF S.L.E.

Multiple sclerosis (MS) can mimic SLE. Between 5 and 10 percent of MS patients have antinuclear or anti-double-stranded DNA antibodies without signs of lupus. On MRI, the lesions of lupus and of MS appear similar, and both the optic nerve (rarely) and the spinal cord may be involved, even repeatedly, in a succession of attacks - feature common for both SLE and MS.

RENAL INVOLVEMENT IN CLINICAL SYNDROMES CLOSELY RELATED TO S.L.E.

All rheumatologic mimickers, drug-induced lupus, Wegener’s granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome, Henoch-Schonlein purpura, anti-GBM vasculitis and sometimes polyarteritis nodosa may mimic renal manifestation of SLE. Renal thrombotic microangiopathy may also mimic active SLE nephritis.

CARDIOPULMONARY MIMICKERS

Dermatomyositis, infections particularly endocarditis, lymphomas, thrombotic thrombocytopenic purpura, immune thrombocytopenic purpura, Still’s disease, and sarcoidosis and other connective tissue disorders may simulate cardiopulmonary manifestations as well as few systemic manifestations of SLE. Toxoplasma pericarditis may also mimic systemic lupus erythematosus.

ENDOCRINOLOGICAL MIMICKER

Seventy-five percent to 90% of patients with Graves’ disease and a smaller percentage of patients with Hashimoto’s thyroiditis have antinuclear antibodies, and many have anti-DNA antibodies as well, despite the fact that overt SLE is uncommon.

CONCLUSION

Though SLE is considered as “great imitator of many diseases”, fortunately there are few conditions which simulate SLE in its dermatological or systemic manifestations. A rational
approach including good history taking, clever physical examinations and targeted serological tests and target organ biopsy often points to the correct diagnosis.

REFERENCES