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Original Research Article

A retrospective study of mucocutaneous lesions of SLE patients and their systemic implications

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ABSTRACT

Background: SLE is a systemic disease with multiorgan involvement occuring very rarely, if so, it has a very grave prognosis if not detected early. Our study enlightens about the evolution of mucocutaneous lesions which can serve as an eye opener for early detection of systemic involvement.
Methods: A descriptive study was conducted in the Department of Dermatology at a tertiary care centre from May 2017 to April 2018 retrospectively. From 15 confirmed cases of SLE a critical retrospective analysis of symptom complex evolution was done and thus a clinical correlation of evolution of mucocutaneous lesions and systemic involvement was attempted.
Results: Out of the fifteen patients in our study comprising various age groups (4-51 years), mean age group was 29.76 years. 14 (93%) were female patients and 1 (6.6%) male patient. Oral ulcerations, Non-scarring alopecia and vasculitic lesions were predominant (3 patients-80%) followed by photosensitivity and cheilitis (9 patients- 60%). Systemic involvement was present in 9 (60%), out of which one (6%) patient had lupus nephritis and 3 patients (20%) had CNS lupus, 2 (13%) had chronic unilateral scleritis, 2 (13%) had interstitial lung disease, one (6%) had coronary heart disease. Mucocutaneous lesions preceded the systemic involvement in 88.8% of cases, with mean duration being 3 years (4 months – 10 years).
Conclusions: Mucocutaneous lesions could serve as an eye opener for diagnosis of SLE, which is always a diagnosis made out of high degree of suspicion apart from certain mucocutaneous lesions serving as an ominous sign of system involvement in SLE.

Keywords: Unilateral episcleritis, Retinal vasculitis, Lupus nephritis, CNS lupus

INTRODUCTION

SLE is a systemic disease characterised by multisystem organ inflammation, most commonly the skin, joints and the vasculature and associated immunological abnormalities. Among cutaneous features photosensitivity, raynauds phenomenon followed by malar rash are the most common presentations according to yell et al.[1] Others include discoid rash, painless oral and nasal ulcers, unilateral episcleritis, livedo reticularis, diffuse alopecia, cutaneous small vessel vasculitis. Abrupt and life-threatening presentations in connective tissue diseases are rarely reported. Ocular involvement though not included in ARA criteria, needs attention as they have served as the forerunners of CNS LUPUS as described by Kalthum et al.[2] Multiorgan involvement

leads to increased mortality.[3] Their early recognition and specific management could change the course of disease.

The first classification criteria was developed by ARA (American Rheumatology Association) in 1982. It included 11 criteria. Though the Systemic Lupus International Colloborating Clinics (SLICC) 2012, includes 17 criteria, it is less specific than ARA criteria for SLE diagnosis. Hence we prefer the old ARA criteria for diagnosis in our study. According to the ACR (ARA) classification, patients must have four of the following eleven manifestations either simultaneously or serially during a given period of observation: 1. Malar rash; 2. Discoid rash; 3. Photosensitivity; 4. Oral ulcers; 5. Arthritis; 6. Serositis (pleuritis or pericarditis);Renal disorder (persistent proteinuria or cellular casts); 8. Neurologic disorder (seizures or psychosis); 9. Hematologic abnormalities (hemolytic anemia, leukopenia, lymphopenia or thrombocytopenia); 10. Immunologic disorders such as anti-dsDNA, anti-Sm or antiphospholipid antibodies (based on IgG or IgM anticardiolipin antibodies, lupus anticoagulant or a serologic test for syphilis false-positive for at least six months); and 11 positive antinuclear antibody test. [3]

This study which is mainly a retrospective descriptive study of confirmed cases of SLE, analyses sequence of cutaneous and mucosal lesions evolving, so as to predict the probability of system/organ involvement. Except for very few occasions like latent lupus nephritis, it has been found in our study that many a times the diagnosis of SLE is made out by the dermatologists, as mucocutaneous lesions are earliest ones to occur irrespective of the system involved. Vasculitis and panniculitis are the pathognomonic histopathological findings of SLE. Cutaneous small vessel vasculitis, when it occurs on a ANA positive background, has to be followed up for a long period of time, as they may turn up as full blown SLE at any point of time. Anti-neutrophil cytoplasmic antibodies should be done at frequent intervals as their positivity is an ominous sign for medium and large vessel involvement, which could turn a benign vasculitis into a major organ failure, thereby turning lethal.

METHODS

A retrospective descriptive study was conducted in the Department of Dermatology at Chengalpattu Medical College (tertiary care centre), Chengalpattu, Tamil Nadu. From the Department's medical records, details of 15 patients with complaints pertaining to connective tissue disorder, of all ages, either sex from May 2017 to April 2018 were collected and included in the study. Mucocutaneous lesions of all these 15 confirmed cases of SLE, were analysed in detail, taking into account the following parameters, namely types of mucocutaneous lesions and their clinical significance as for as system or organ involvement is concerned. Out of the 15 patients of the study population we are highlighting the mucocutaneous lesions of 5 patients in detail which strongly has a correlation with the organ/system involved.

Institutional ethical committee clearance was obtained prior to the commencement of the study and informed consent was taken from the participant patients in regional language. Clinically patients with other photosensitive disorders like porphyrias, xeroderma pigmentosum and overlap connective tissue diseases like scleroderma (progressive systemic sclerosis) and mixed connective tissue disorders were excluded. A diagnosis of SLE was made based on the clinical criteria, ARA criteria (4/11) either at one point of time or over a period of 6 months one after the other. Immunological criteria observed were positive ANA and dsDNA titre, false positive VDRL for more than 6 months, C3 and C4 levels and Histopathological findings under H&E section observed were fibrinoid necrosis, collagen sclerosis, necrosis and basophilic bodies formation and features of panniculitis and vasculitis. All the patients were started on with Tab. Hydroxychloroquine after obtaining ophthalmology opinion regarding macular status and color vision, in a dosage of 6.5 mg/kg body weight given in two divided doses, systemic steroids used in our study were Tab. prednisolone 1 mg/kg body weight till clinical resolution, the mean duration being 6 weeks, care was taken to ensure morning dose was higher than night dose to accomadate circadian rhythm, other steroids used were methylprednisolone pulse 1 gm given I.V. in 500 ml of normal saline over 4 hours in 3 successive days and the anti-epileptic used was levetiracetam (for CNS lupus), the dosage of which was as per the neurologists suggestion. Convenient sampling size was used as this is a rare disease. In all these 15 cases, a critical retrospective analysis of symptom-complex evolution was done and thus a clinical correlation of evolution of mucocutaneous lesions and systemic or organ involvement was attempted. Appropriate statistical calculations were incorporated, as per standard norms and the patients were studied using an appropriate univariate analysis.

Statistical analysis used

Appropriate statistical analysis using SPSS 22 software was done and mean, median were calculated wherever applicable. Analysis used was univariate analysis.

RESULTS

Out of the fifteen patients in our study comprising various age groups (4-51 years), mean age group was 29.76 years. 14 (93%) were female patients and 1 (6.6%) male patient. The duration of illness at presentation varied from 10 days to 5 years and the mean duration at presentation was 12 months) as mentioned in Table 1). Oral ulcerations, Non-scarring alopecia and vasculitic lesions (Figure 2 A and B, 3) were predominant (12 patients - 80%) followed by malar rash (Figure 4 A), photosensitivity and cheilitis (9 patients - 60%), ocular involvement, facial edema, DLE – (Figure 5) (3 patients - 20%). Ocular involvement was a ominous forerunner of CNS lupus, which was present in 2 patients (13%). Systemic involvement was present in 9 (60%), out of which one (11.1%) patient had lupus nephritis and 3 patients (33.3%) had CNS lupus, 2 (22.2%) had chronic

unilateral scleritis (Figure 6), 2 (22.2%) had interstitial lung disease, one (11.1%) had coronary heart disease)as mentioned in Figure 8). Mucocutaneous lesions preceded the systemic organ involvement in eight out of nine cases (88.8%), with mean duration being 3 years)varying from 4 months – 10 years). Out of them, 7 patients were under remission with hydroxychloroquine and prednisolone 10mg maintenance dose, 3 patients were released from treatment and are under follow up, 5 patients with exacerbation of the disease, under treatment. In histopathology, all patients had Fibrinoid necrosis, collagen sclerosis, necrosis and basophilic body formation. Both panniculitis and vasculitic pictures were observed under H&E section (Figure 7). Thus it is clearly obvious, that even though SLE is a disease that demands synchronised multidisciplinary management logistics, its only the Dermatologist who has to play the crucial lead role of diagnosing SLE.

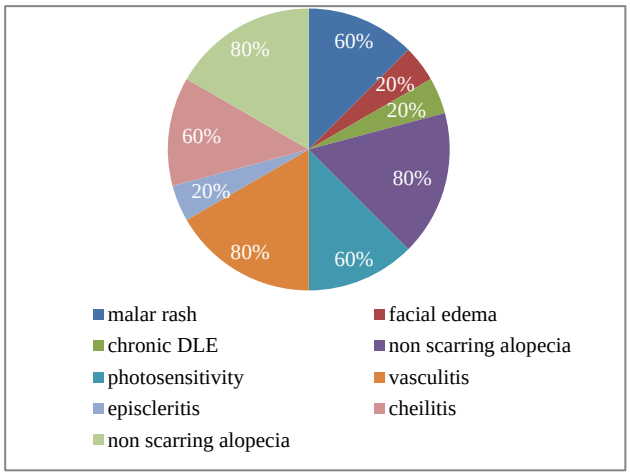

Figure 1: Cutaneous features in our study.

Figure 2: (A) Malar rash, vasculitic lesions & lip erosions in lupus nephritis patient; (B) Lip and oral erosions.

Table 1: Showing demographic data.

Demographic data	Mean
Age	29.76 years
Male	1(6.67%)
Female	14 (93.3.50
Duration at presentation	12 months

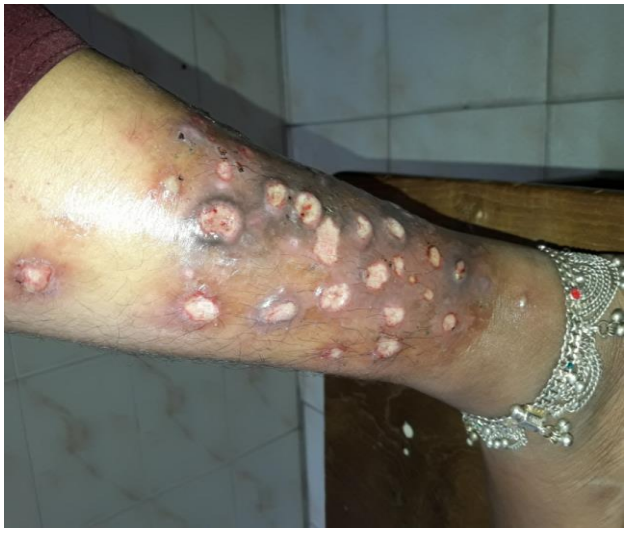

Figure 3: Multiple non healing vasculitic ulcers – lower 1/3rd leg.

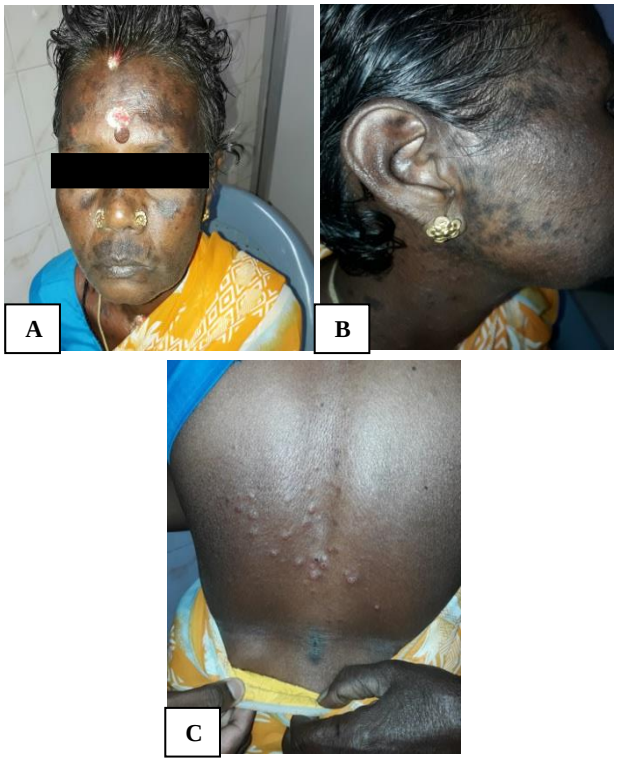

Figure 4: (A) Vasculitic lesions & malar rash (sparing of nasolabial fold is seen); (B and C) vasculitic lesions over sidelocks & lower back.

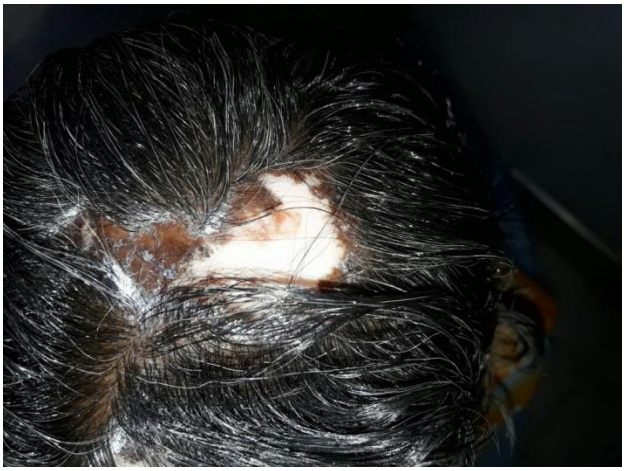

Figure 5: DLE lesion over scalp.

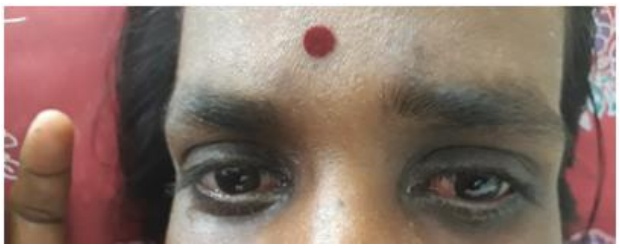

Figure 6: Episcleritis of left eye preceding CNS LUPUS.

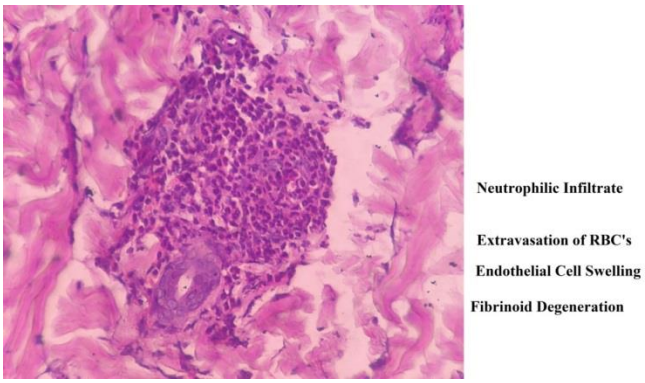

Figure 7: HPE showing leucocytoclastic vasculitis.

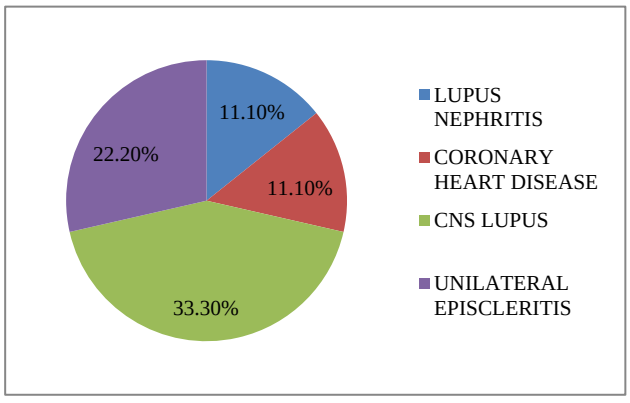

Figure 8: Systemic involvement.

DISCUSSION

SLE is a systemic disease characterised by multisystem organ inflammation, most commonly the skin, joints and the vasculature and associated immunological abnormalities, but systemic multiorgan involvement may occur with increased mortality.[3] Abrupt and life-threatening presentations are rare in connective tissue diseases and among this SLE is one main entity so their early prompt recognition and specific treatment could change the course of disease. The first classification criteria were developed by ARA (American Rheumatology Association) in 1982.[3] It included 11 criteria. Though the systemic lupus international collaborating clinics (SLICC) 2012, includes 17 criteria, it is less specific than ARA for SLE diagnosis. Hence we prefer the old ARA criteria for diagnosis in our study

Pathogenesis

SLE is believed to be a complex interplay of genetics, infectious and immunologic factors. It has a concordance rate of 30-50% in monozygotic twins and the implicated HLA associations being HLADR2, HLA-DR3, HLA-B7, HLA-B8.[4] Various viruses, drugs and environmental triggers have been implicated to induce molecular mimicry.[5] Apart from classical antibodies seen among SLE patients, newer autoantibodies are now implicated in patients with SLE, including antibodies against annexins, CD 45 cell surface glycoprotein, calreticulin and nucleosomes.[6-8] In a study done by The Department of Defense Serum Repository.[9] Approximately over 30 million specimens were prospectively collected, from more than 5 million U.S. Armed forces personnel. In this study it was found that in 115 of the 130 patients with SLE (88%), atleast one of the SLE autoantibody tested was present 9.4 years earlier before the diagnosis could be made clinically, thereby proving that these autoantibodies are literally present many years before clinical diagnosis of SLE could be made.

Clinical presentations

Mucocutaneous lesions are the initial manifestation and also the forerunners of systemic activity in 80% of SLE cases.[10-12] The clinical features and the mucocutaneous lesions of SLE of our study population are discussed in figure1, which correlates with already published data as adapted from Yell et al, and it very well correlates with the results obtained in our study.[1] The American College of Rheumatology (ACR) defines 19 distinct clinical central and peripheral neuropsychiatric syndromes that can occur in SLE, twelve of which are due to CNS involvement.[13] These syndromes can precede other symptoms of SLE or may occur at any point during the course of the disease, thus, the clinical course is extremely unpredictable.

Urticarial vasculitis can be parted into two types, those with normal complement levels and those with

hypocomplementemia associated. The latter likely has systemic manifestations and they have a possibility of progression towards SLE.[14] Sometimes, a hypo-complementemic patient initially diagnosed with an idiopathic hypocomplementemia urticarial vasculitis has an underlying disease such as SLE but normo-complementemic urticarial vasculitis is not rarely associated with SLE.

Anti-dsDNA antibodies can be detected atleast 2 years before diagnosis of clinical disease. Serum anti-dsDNA antibody levels is a ominous predictor of lupus nephritis patients, as shown by study done by Chan which is also proven in our study.[15]

Nephritogenic anti-dsDNA antibodies regulates gene expression of inflammatory and fibrotic mediators in resident renal cells and exerets a direct effect on kidney inflammation and fibrosis. The precise mechanism is not fully defined, but the data to date suggest that they either bind directly to cross-reactive antigens on the surface of resident renal cells or to components of the extracellular matrix, or indirectly through binds to nucleosomes of constituents of the glomerular basement membrane. Any female patient of SLE who turns positive for Ro/SSA, on extractable nuclear antigen vira strip test, on entering family way runs the risk of begetting a neonatal lupus child. On an average 98% of affected infants have maternal transfer of autoantibodies against Ro/SSA, La/SSB, and, less frequently U1-RNP. The 52-kD Ro/SSA ribo-nucleoprotein is strongly linked in the autoimmune response in mothers whose children have congenital heart block.[16] These autoantibodies antagonize the serotonin-induced L-type calcium channel activation on human fetal atrial cells and trigger an inflammatory, leading to fibrosis and scarring of the atrioventricular node, sinus node, and His bundle. This explains the electrophysiological abnormalities of the cardiac rhythm disturbances, which may lead to the subsequent congestive heart failure.

Ocular manifestations of SLE is seen in one third of patients. SLE if left untreated, can lead to significant visual loss or even blindness. When lupus retinopathy or neuro-ophthalmic involvement is detected in a patient, a thorough search for systemic involvement is necessary as it may reflect systemic involvement, particularly vascular and CNS damage, as described by Kalthum et al.[2] Our study had ocular involvement in 13% patients.

Cotton-wool spots, the classic lesions of lupus retinopathy occur due to the background occlusion of the small retinal arterioles, or end arterioles, by infiltrating inflammatory cells, leading to the interruption of axoplasmic flow within the nerve fiber layer of the retina, resulting in swelling of the nerve fiber. The patients may be completely asymptomatic or may have visual loss with macular involvement. On fluorescein angiography, areas of focal nonperfusion are seen. In contrast to retinal nonperfusion from hypertension and diabetes, the ischemia produced here is often not as extensive and is not associated with widespread arterial narrowing.[17,18]

Although ocular manifestations is one of the features of SLE, sometimes even the initial presentation, they are not included among the 11 ARA criteria; we believe this is an oversight and further, its inclusion among the diagnostic criteria for SLE would enable earlier diagnosis and management in some instances.

Close communication between the vigilant ophthalmologist and the treating consultant is critical in the effective management of these complex clinical situations for both diagnosing retinal involvement and for starting hydroxychloroquine which warrants the colour vision and macular status of the patient, before initiating the therapy, as long term administration could lead on to Bulls eye maculopathy.[19] Early stages of TB and SLE very much mimic each other as Erythema nodosum like lesions, maculopapular lesions of vasculitis can occur in both. High degree of suspicion and Gene Xpert helps to differentiate both. [20]

Cutaneous small vessel vasculitis, when it occurs on a ANA background, has to be followed up for a long period of time, as they may turn up as full blown SLE at any point of time. ANCA should be done at frequent intervals as their positivity is an ominous sign for medium and large vessel involvement.

Limitations

Our study was limited by its small sample size and shorter duration of follow up. Studies on larger sample size with longer duration of follow up would enable us a better enlightment of the progression of disease course.

CONCLUSION

This study depicts that mucocutaneous lesions could serve as an eye opener for diagnosis of SLE, which is always a diagnosis made out of high degree of suspicion apart from certain mucocutaneous lesions serving as an ominous sign of system/organ involvement in SLE.

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Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Lee LA. Cutaneous lupus in infancy and childhood. Lupus. 2010;19:1112–7.
2. Md Noh UK, Zahidin AZA, Yong TK. Retinal vasculitis in systemic lupus erythematosus: an indication of active disease. Clin Pract. 2012;2(2):54.
3. Rowell NR. Some historical aspects of skin disease in lupus erythematosus. Lupus. 1997;6:76–83.

4. Abbas AK, Lichtman AH, Pober JS. Self tolerance and autoimmunity. 2nd edn. In: Cellular and Molecular Immunology. 1994: 384.
5. McClain MT, Heinlen LD, Dennis GJ, Roebuck J, Harley JB. Early events in lupus humoral autoimmunity suggest initiation through molecular mimicry. Nat Med. 2005;11:85-9.
6. Bastian BC Annexins in cancer and autoimmune diseases. Cell Mol Life Sci. 1997;53:554-6.
7. Mamoune A, Saraux A, Delaunay JL, Le Goff P, Youinou P, et al. Autoantibodies to CD45 in systemic lupus erythematosus. J Autoimmun. 1998;11:485-8.
8. Boehm J, Orth T, Van Nguyen P, Söling HD Systemic lupus erythematosus is associated with increased auto-antibody titers against calreticulin and grp94, but calreticulin is not the Ro/SS-A antigen. Eur J Clin Invest. 1994;24:248-57.
9. Arbuckle MR. Development of Autoantibodies before the clinical onset of Systemic Lupus Erythematosus. N Engl J Med. 2003;349:1526-33.
10. Kabin DI, Malkinson FD. Lupus erythematosus and calcinosis cutis. Arch Dermatol. 1969;100:17–22.
11. Pramatarov K. Discoid lupus erythematosus of the soles. J Dermatol. 1989;16:511.
12. Rowell NR. The natural history of lupus erythematosus. Clin Exp Dermatol. 1984;9:217–31.
13. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1982;25:1271–7.
14. Her MY, Song JY, Kim DY. Hypocomplementemic Urticarial Vasculitis in Systemic Lupus Erythematosus. J Korean Med Sci. 2009;24(1):184-6.
15. Yung S, Chan TM. Mechanisms of Kidney Injury in Lupus Nephritis –the Role of Anti-dsDNA Antibodies. Frontiers Immunol. 2015;6:475.
16. Lun Hon K, Leung AKC. Neonatal Lupus Erythematosus. Autoimmune Dis. 2012;2012:301274.
17. Dougal MA, Evans LS, McClellan KR, Robinson J Central retinal artery occlusion in systemic lupus erythematosus. Ann Ophthalmol. 1983;15:38-40.
18. Goldstein I, Wexler D Retinal vascular disease in a case of acute lupus erythematosus disseminatus. Arch Ophthalmol. 1932;8:852-7.
19. Goldman FD, Gilman AL, Hollenback C. Hydroxychloroquine inhibits calcium signals in T cells: a new mechanism to explain its immunomodulatory properties. Blood. 2000;95(11):3460–6.
20. Prabu VN, Agrawal S. Systemic lupus erythematosus and tuberculosis: A review of complex interactions of complicated diseases. J Postgraduate Med. 2010;56(3):244–7.

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