Original Article

Surreptitious Tales Of Systemic Lupus Erythematosis (Sle)

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Abstract

Systemic lupus erythematosus (SLE) is an auto-immune, multi-systemic inflammatory disease affecting various major organs in the body. This is an interesting case series on unanimous presentations of SLE in a tertiary care centre. This case series gives an idea of approaching wide variety of clinical manifestations as initial symptoms in SLE. All 5 cases have been diagnosed with American college of Rheumatology criteria. A young female with GTCS seizures as a presenting symptom was diagnosed as CNS lupus finally. Initial symptoms like seizures, cognitive impairment, anxiety can also give the path-breaking clues to neuropsychiatric SLE. One of the causes of pyrexia of unknown origin (PUO) is connective tissue disorders, although SLE is common among them, SLE presenting with gastro-intestinal symptoms in PUO is very rare. After reviewing literatures, only very few cases of male SLE reported and eventually, the proteinuria was evaluated and diagnosed to have minimal change disease in renal biopsy in an 18yr old boy. Patient was temporarily dialysed and started on pulse-steroids and his renal functions restored gradually. SLE can also present with other connective tissue disorders like Sjogren's syndrome, scleroderma, rheumatoid arthritis. Anti-RNP antibodies in higher titres in SLE patients supports the diagnosis of mixed connective tissue disorders (MCTD). Although it has a multi-system involvement, diffuse alveolar heamorrhage (DAH) as clinical presentation is life-threatening and very rare and only 2% cases reported in SLE. Among the 5 cases,4 cases survived with I.V pulse-steroids and immune-modulators, while one patient with DAH succumbed to death.

Keywords: Systemic lupus erythematosis, Pyrexia of unknown origin, Diffuse Alveolar Haemorrhage, Mixed Connective Tissue Disorder, CNS lupus, lupus nephritis

INTRODUCTION

This case series is based on various clinical presentations of SLE and how to approach and cornering the diagnosis. In SLE, the immune system is chronically and repeatedly activated, which leads to the creation of antibodies and other protein products that cause tissue destruction and inflammation. In India, among every 1,00,000 population, 3.2 is the prevalence rate for SLE[1] and globally it varies from 6.50 to 175 per 1,00,000 cases [2]. It often starts in a female's reproductive age and mostly affects women with a higher preponderance ratio (9:1). Genetic variations, mutations, complement deficiencies, environmental and immune (innate & adaptive) factors plays a pivotal role in the pathogenesis of SLE[3]. The pathogenesis of SLE has historically centred on the immune complexes that accumulate in the skin, kidneys and other regions of tissue destruction, as well as a putative role for direct antibody targeting of regional or planted antigens[4]. It is a multi-system disease mainly involving skin, joints and connective tissues, renal, neurological, pulmonological, cardiac systems[3].Based on the clinical features, auto-antibodies and EULAR/ACR criteria diagnosis is made[5].In this case series, we present various cases of SLE with a myriad of clinical manifestations.

Case 1:

26year old woman was brought to casuality with complaints of focal seizures 2 episodes followed by altered sensorium. Patient had previous history of anxiety disorder and hypothyroidism for which she was on therapy and regular medications for past 2 months. She also gave history of small joint pains with stiffness for 4 months for which she was on native medications. There was no h/o fever, vomiting, neck stiffness, head injury. On examination, patient was drowsy, disoriented, afebrile, pallor+, poorly nourished. Bp-110/70mmhg, pr-96/min, rr-22/min, spo2-99%, cbg-108mg/dl .On local examination, hyperpigmented rash was present over the malar region with crusted plaques and scaly lesions over scalp, face, ears with hyperpigmented macules in palms and soles.**(Figure 1 & 2)**

On CNS examination patient, Mini Mental scoring (MMSC) was 19, cranial nerve examination was normal. On motor examination, patient had resting tremors with choreiform movements in upper limbs. Bilateral plantar were flexors and Rhomberg's test was negative. Patient had no signs of meningeal irritation.
Serology showed Hb-8.4, MCV-85, peripheral smear shows mixed microcytic, normochromic and normocytic anemia. ANA positive 4+ homogenous pattern, anti-sm ab positive, anti-ds dna positive, c3 and c4 compliments are low. CT brain shows no evidence of hemorrhage or infarct or space occupying lesions. CSF analysis shows higher protein and glucose levels along with anti-ribosomal p antibody. Sledai score showed severe disease activity. MRI brain shows discrete T2/T2 flair hyperintensities in Periventricular and deep white matter of left parietal region with small vessel ischemic changes and mild cerebral atrophy with features suggestive of cns lupus **(Figure 3).**

A diagnosis of SLE with CNS lupus was made and patient was started on steroids, antiepileptics, antibiotics, Thyroxine and HCQ's. Patient sensorium levels, rashes, anemia and seizures improved after starting treatment and now she is in regular follow up.

Case 2:

32yr old women, known case of hypothyroidism came to medicine opd with complaints of high grade fever associated with chills, headache and loose stools for 7 days. Patient also had generalised myalgia. Patient denied history of drugs, native medication, rashes, arthralgia, vomiting, neck stiffness, blurring of vision, dyspnoea, chest pain, palpitation or abdominal pain. On Examination, Patient is concious, oriented, febrile+, pallor+, moderately nourished. No cyanosis, clubbing, lymphadenopathy, pedal edema. Vitals: BP-100/70mmhg, PR-116/min, RR-22/min, SPO2-99%,CBG-98mg/dl,Temp-102*F. Sytemic examination was normal and unremarkable. No signs of meningeal irritation.

On day 1 patient had history of high-grade fever with 2 episodes of loose stools. Initial blood investigations shows Hb-8.2,wbc-3530,platelets-1,43,400.ESR-64,CRP->130mg/dl,TFT-normal,D-Dimer-859,fibrinogen-408.5mg/dl,Ferritin-2420,Serum LDH-283, Total bilirubin-0.33, direct-0.09, AST-348, ALT-123.Peripheral smear shows normocytic normochromic anemia. Bone marrow shows mild erythroid and myeloid suppression with few atypical cells with increased nuclear and cytoplasmic ratio with normal plasma cells and morphology. Fever profile was negative for dengue, malaria, typhoid, scrub-typhus, leptospirosis. Blood cultures (2 different sites), bone marrow, urine cultures, stool cultures were negative. X-ray chest was normal. USG abdomen and 2D echo screening was normal. Patient was initially started on broad spectrum antibiotics, IV fluids, antipyretics. Fever was not subsided since the time(6^{th} day) of admission and due to high grade fever, anemia, thrombocytopenia and in suspicion of clinical malaria patient was started on antimalarial drugs and inspite of it fever continued and patient was further evaluated for pyrexia of unknown origin. HRCT chest which was showing focal areas of subtle ground glassing in superior segment of right lower lobe with atelectatic changes in posterior segment of right upper lobe, medial and lateral segments of right middle lobe, lateral basal segment, inferior lingular segment and posterior basal segments of bilateral lower lobes,CORADS-2.Covid-19 RT-PCR, covid IgM, IgG Ab were negative. Viral serology was negative. Ebstein barr virus (EBV) IgM-Ab was negative. Sputum for AFB, gram stain, cultures, fungal KOH mount, CBNAAT, ADA was negative. CT abdomen shows subcentimetric calcified granuloma in left lobe of liver and few subcentimetric mesenteric lymph nodes with mild haziness along root of mesentry with few small left para-aortic lymph nodes measuring ~14.5*9 mm. On 10^{th} day, patient was planned for CT guided lymph node biopsy to rule out TB abdomen vs malignancy and unfortunately patient sensorium deteriorated, drowsy, disoriented and agitated. Emergency CT brain followed by MRI brain was done which was normal. Serum electrolytes were unremarkable. CSF analysis shows high protein and glucose levels with ocassional lymphocytes. Patient was shifted to medical ICU. Being an young female presenting with atypical course of fever, pancytopenia, altered sensorium and with above imaging findings auto-immune diseases were suspected and ANA profile was done which shows ANA-3+ Speckled pattern, 1:80 dilution. Anti-ds DNA, anti-sm Ab was positive. ACR and EULAR criteria score was 23.Patient was started on pulse doses of methyl prednisolone followed by which patient sensorium improved and was discharged with oral prednisolone and in regular follow up.

Case 3:

An 18yr old boy with no known comorbidities came to medicine opd with complaints of facial puffiness and swelling of lower limbs for 1 week. He had a history of reduced urine output for 1 day. He denied history of fever, sore throat, arthralgia, rashes. He had no history of NSAID abuse or native medications. On examination, patient is conciouss, cooperative, moderately built and nourished, anasarca present,afebrile,BP-100/60mmhg,PR-108/min,RR-18/min,SPO2-97%,CBG-87mg/dl.Patient was evaluated in hospital and initial baseline investigations shows ESR-48, CRP-112mg/dl, ASOtitres-120, serum albumin-8.5g/dl, urea-50, serum creatinine-4.2mg/dl, serum potassium-5.5meq/l,bicarbonate-18meq/l, urine protein was 3+, urine red blood cells-2+, urine spot PCR-2.6,24 hours urine protein-2.8g/dl. Serum electrophoresis shows prominent alpha 2 macroglobulin band with low albumin bands. USG abdomen shows raised renal cortical echoes with well-maintained cortico medullary differentiation.

Screening auto-immune workup was done which shows ANA-4+ homogenous pattern, anti ds-DNA and anti-sm Ab was positive. Complements C3,C4 levels were normal. Percutaneous renal biopsy was performed and sent for histopathological examination. On day3 of admission, serum creatinine increased to 5.6mg/dl, serum potassium-5.8meq/l, urine output was <0.3ml/kg/hr in 24 hrs. In view of raised creatinine levels, hyperkalemia and reduced urine output, patient was started on temporary dialysis. Renal biopsy in light microscopy revealed 8 glomeruli in renal cortex, out of

which two are globally sclerotic and mesangial hyper cellularity seen in the viable glomeruli and segmental sclerosis is identified in one glomerulus and rest of glomeruli are unremarkable. No spike formation or active lesions on glomerular basement membrane. No evidence of necrotising lesions are crescent formation. There is evident cytoplasmic swelling and vacuolation in the tubular epithelial cells **(FIGURE 4).** Immunoflourescence was negative. There is mild mesangial proliferation in glomeruli and tubular epithelial damage by lymphocytes as well established. Final impression was Acute tubular injury with Minimal change disease. Patient was started on pulse doses of corticosteroids and cyclophosphamide followed by which renal parameters drastically reduced and patient was discharged with oral cortiocsteroids and immunomodulators and was in current follow up.

Case 4:

A 42 yr old female without any comorbidities was brought to casuality with complaints of abdominal distension, lower limbs swelling, dyspnoea on exertion for 1month and history of facial puffiness, oliguria, scaly lesions over trunk and back for 15 days. She had history of low grade fever on off episodes for 1week.She also had history of dry mouth and dry eyes for 3months.On examination, patient was conciouss, oriented, febrile, pallor & bilateral pitting pedal edema present. Erythematous crusted erosions with few targetoid lesions seen over the trunk and upper back **(Figure 5).**No icterus, cyanosis, clubbing, lymphadenopathy or raised JVP.BP-120/80mmhg,PR-108/min,RR-22/min,SPO2-99%,Temp-100*F,CBG-110mg/dl.Systemic examination shows distended abdomen with mild ascites without any warmth, tenderness, guarding, rigidity or organomegaly. Baseline investigations shows Hb-9.8g/dl,wbc-3,500cells/mm^3,platelets-1,50,000,coagulation profile was normal,ESR-80,CRP-28mg/dl,RF-positive,anti-CCP-negative,peripheral smear shows normochromic normocytic anemia with leukopenia, total protein-6.2g/dl,albumin-1.5,globulin-4.7,serum creatinine-0.5mg/dl,urea-46,k+-3.9meq/l,Na-136meq/l,HCO3-18.1meq/l,cl-98.urine protein-1+,24hrs urine protein-982mg/dl, USG abdomen showing mild ascites without any collaterals or hepatosplenomegaly with normal kidney size. X-ray shows costophrenic angle blunting bilaterally. Serum electrophoresis shows hypo-albuminemia bands. With above clinical and laboratory evidence ANA profile was done and surprisingly shows ANA-3+,1:100 dilution with fine granular pattern, anti-SM ab-positive, anti-SSA-positive, Ro-52-positive, SSB-weak positive, RNP/sn-positive, nucleosomes-weak positive,AMA-M2-strong positive. Viral serology-negative. In view of suspicion of SLE with overlapping sjogrens, Shirmers test was positive (<5mm) with which we came to the diagnosis of SLE with overlapping Sjogrens syndrome.

Case 5:

A 48 yr old female who is known case of SLE with lupus nephritis stage-4 since 3yrs was brought to the casuality with complaints of dyspnoea grade 4 MMRC, bilateral lower limb swelling, oliguria since 3 days. On admission,BP-140/80mmhg,PR-118/min,RR-36/min,SPo2-90% under room air, On examination, patient was conciouss, oriented, tachypnic, bilateral pitting pedal edema, scaly erythematous crusted lesions seen all over face, ears and scalp region. Sytemic examination shows S1,S2 present, no murmur, RS-bilateral coarse crackles diffusely in all areas of the lungs, P/A-soft, distended, mild ascites, no organomegaly clinically, CNS-NFND. Lab investigations shows Hb-8.4,T.C-16,680,N-93,L-5.8,E-1.1,B-0,Platelets-1,30,000, MCV-83,PCV-26, creatinine-4.2, Urea-199, BUN-93, Na+-132,k+-4.6, Hco3-23, cl-100,RBS-125,Total bilirubin-1.9,PT-14,APTT-36,INR-1.1,USG raised renal cortical echoes with poorly maintained corticomedullary differentiation. ANA 4+ homogenous pattern, anti-sm ab positive, anti-ds DNA positive, ESR-48, CRP-32mg/dl. Patient was initially admitted in ICU and was dialysed twice in view of raised creatinine levels and reduced urine output. Patient was started on I.V mycofenolate mofetil (MMF).Urine routine had 10-12 pus cells, urine culture shows significant colony count(1,00,000) of E.coli and Enterococcus which was sensitive to Teicoplanin. MMF was stopped in view of sepsis and raised procalcitonin levels. Over the course of period, patient gradually improved and hemodynamically stable and was shifted to medical ward. On day 3 of stay in the ward, patient developed sudden onset of hemoptysis, dyspnoea, tachypnoea and SPO2 levels dropped to 88%,BP-100/60mmhg,patient was started on oxygen support, IV fluids and shifted back to medical ICU.X-ray chest shows diffuse air space opacities with consolidatory changes involving bilateral lung fields **(FIGURE 9).** CT-Chest shows patchy areas of ground glass opacities in bilateral lung fields, predominantly in peri broncho-vascular areas with bilateral mild pleural effusion (right >left) with mild extension with sub-segmental collapse of underlying segments also with mild pericardial effusion. Imaging was suggestive of Diffuse alveolar heamorrhage (DAH).Patient was started on Inj. Tranexamic acid to arrest bleeding. She was tachypnoeic with 15 litres of NRBM and was started on NIV/CPAP support, on day4, patient was intubated and connected to mechanical ventilatory support in view of desaturations and altered sensorium. Patient was given one schedule of I.V Plasmapheresis. On day5, BP was not recordable and patient was started on ionotrope supports and increased to triple supports with maximum doses. Patient went into cardiac arrest and inspite of all resuscitation measures, she was declared to be dead.

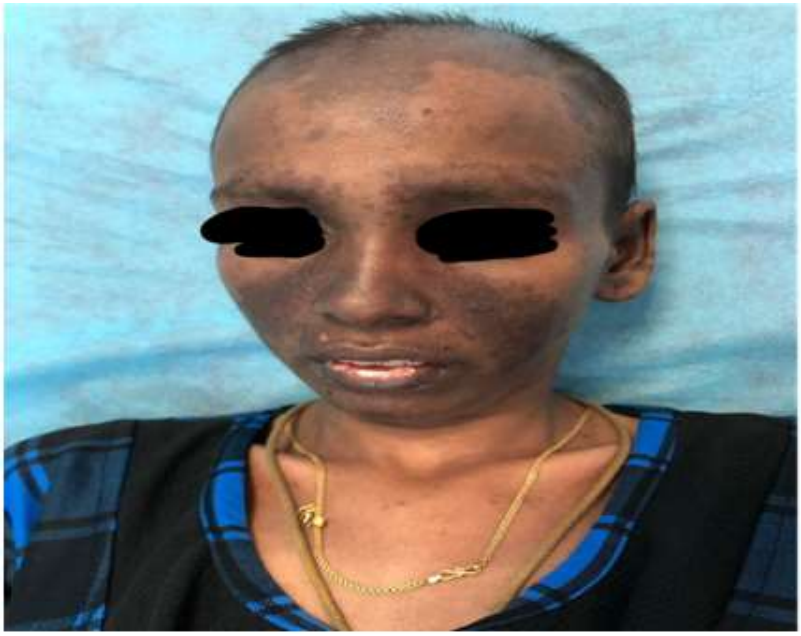

FIGURE 1: Shows typical malar rash and cutaneous lupus lesions in SLE patient.

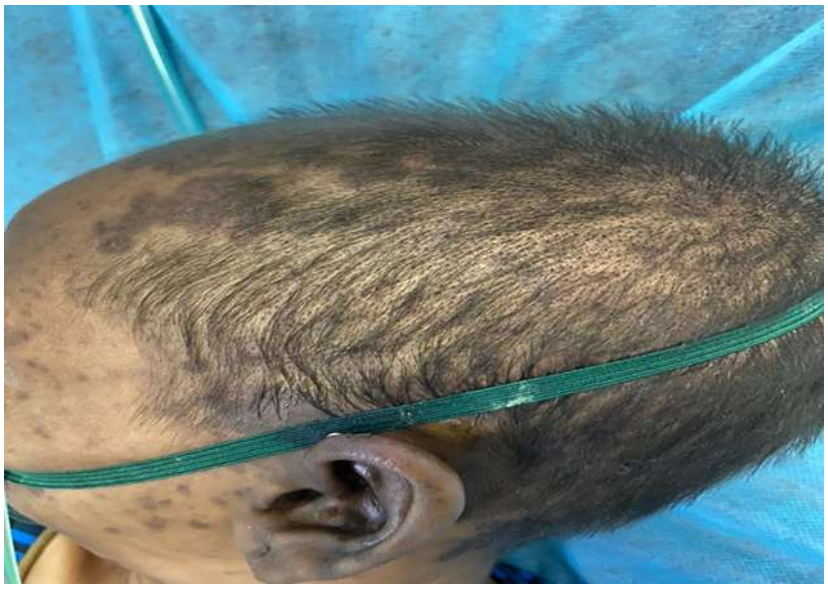

FIGURE 2: Shows non-scarring alopecia with crusted hyperpigmented lesions over pinna and face.

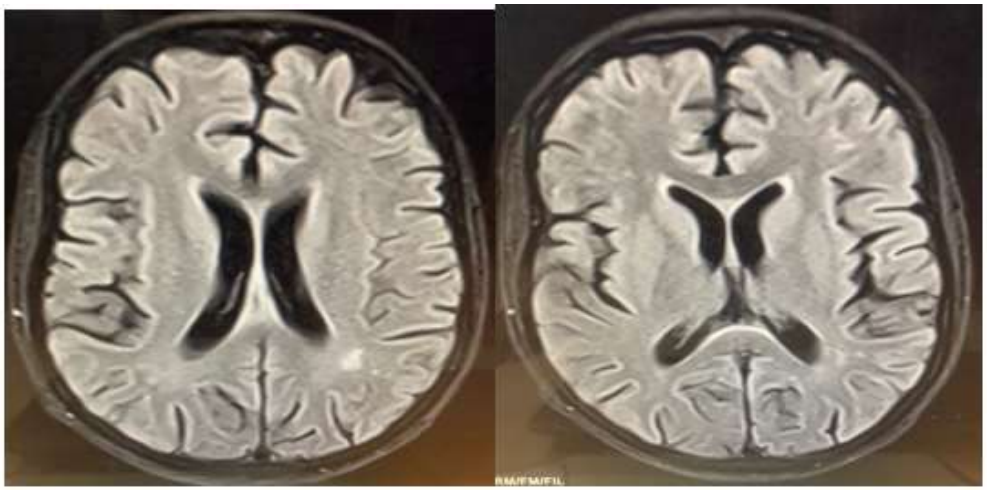

FIGURE 3: MRI brain shows discrete T2/T2 flair hyperintensities in periventricular and deep white matter in bilateral parietal areas.

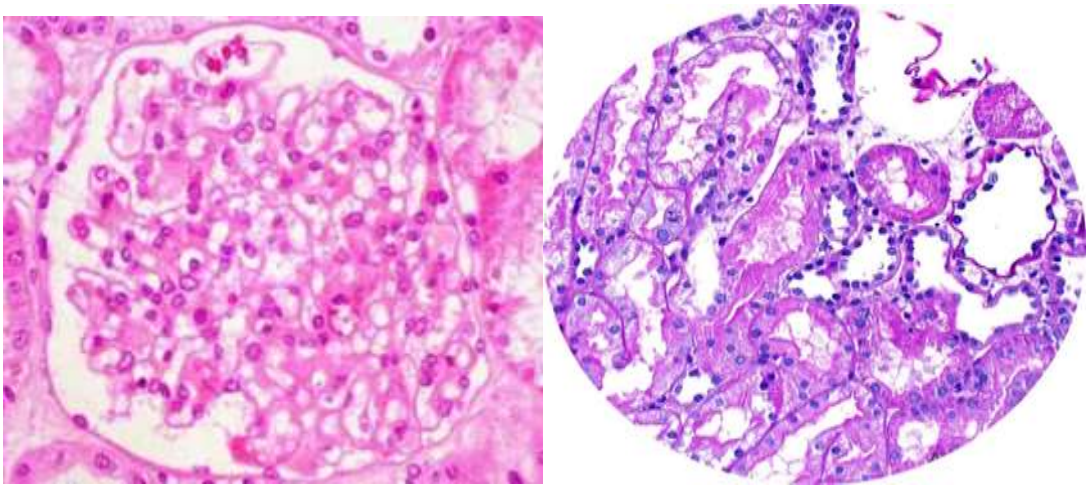

Figure 4: shows Light microscopic image of mesangial proliferation with cytoplasmic swelling and vacuolation in the tubular epithelial cells.

FIGURE 5: Shows Erythematous crusted erosions with few targetoid lesions seen over the trunk and upper back in a SLE overlapping sjogrens syndrome patient (MCTD).

FIGURE 6: Shows scaly hyperpigmented crusted lesions seen all over face, ears and scalp regions in acute cutaneous lupus patient [ACLE]

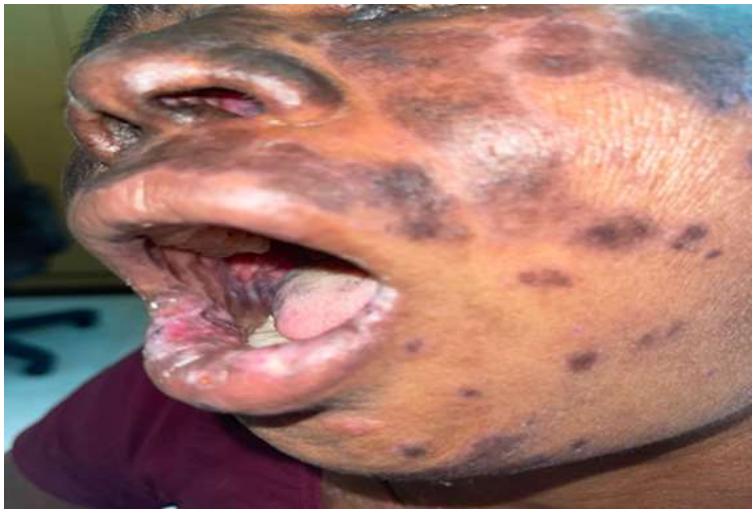

FIGURE 7: Oral mucosa showing erythematous lesions over the palate and buccal mucosa

FIGURE 8: Shows multiple hyperpigmented plaques over the scalp and diffuse thinning of hair in ACLE patient

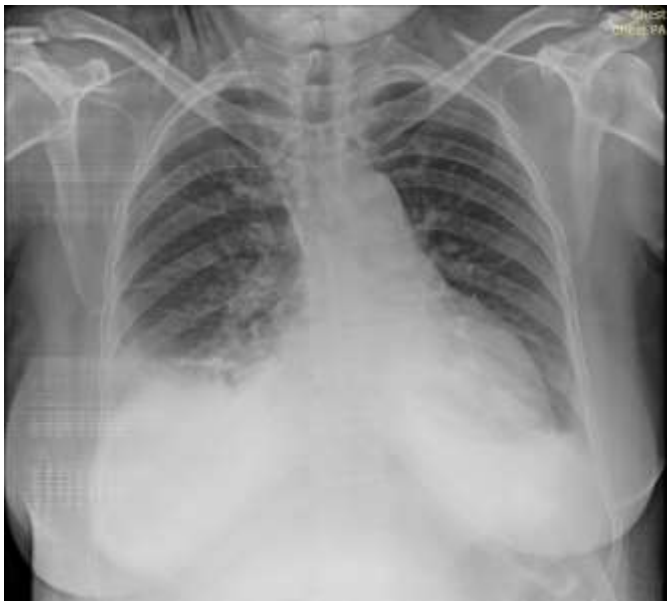

FIGURE 9: X-ray chest shows diffuse air space opacities with consolidatory changes involving bilateral lung fields, along with bilateral pleural effusion

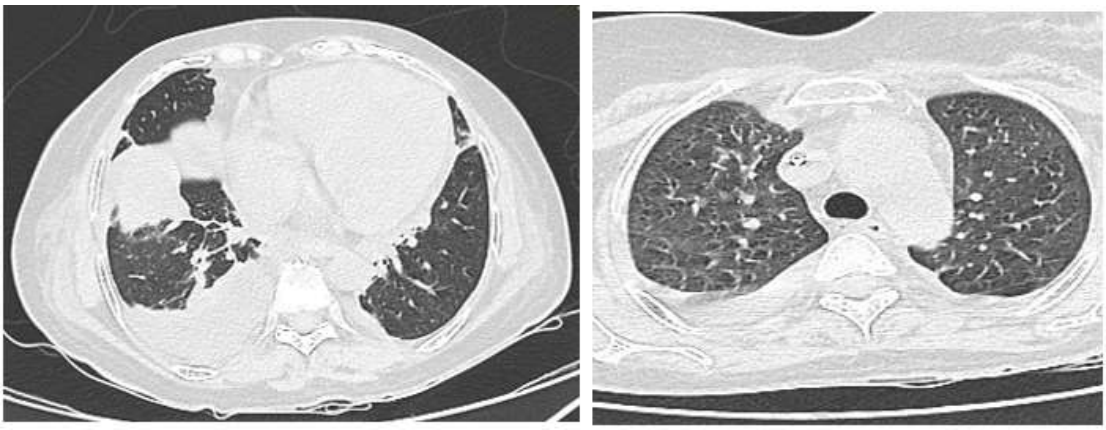

FIGURE 10: CT-Chest shows patchy areas of ground glass opacities in bilateral lung fields, predominantly in peribronchovascular areas with bilateral mild pleural effusion (right >left) with fissual extension with sub-segmental collapse of underlying segments suggestive of Diffuse alveolar heamorrhage (DAH)

DISCUSSION:

SLE is an auto-immune as well as multi-factorial, multisystemic inflammatory disease particularly involving skin, connective tissues, joints and widely to kidneys, lungs, heart and brain. SLE is diagnosed using EULAR/ACR criteria[5].In this discussion, there are 5 cases of various rare presentations of SLE, out of which 4 cases are newly diagnosed.(Case-1) deals with atypical presentation of a GTCS type of seizures which was later diagnosed as a neuropshychiatric manifestation of SLE. The prevalence of Neuropsychiatric manifestations in SLE(NSPLE) varies from 18 % to 37% globally [6].More than 50% of cases can present with headaches, anxiety disorders and cognitive disturbances.[7] NSPLE is mostly associated in patients who are on immunosuppresants and steroids and eventually have a poor quality of life.[8,9] but in our case patient gradually improved with I.V pulse steroidal therapy and MMF and was in regular follow up.(Case-2) deals with a rarest presentation of pyrexia of unknown origin (PUO). In a case study done by *Handa R et al [10]* " a total of 121 PUO cases were evaluated for causes out of which 15.7% were diagnosed to have collagen vascular diseases and connective tissue disorder". There also cases reported in PUO presenting as SLE induced pericarditis.[11,12] In our scenario patient gradually improved with I.V Pulse steroid therapy and in regular follow up.(Case-3) is an unanimous case of male SLE presenting as acute tubular injury with minimal change disease. The prevalence of minimal change disease is only 0.93% in SLE patients. *Lei-Shi et al [13]* "did an analysis with 13,519 renal biopsies which shows SLE as the most common cause sor secorndary glomerulonephritis". *Dube GK et al [14]* "in his study (N=7) patients presented with full blown anasarca, nephrotic-range proteinuria and biopsies revealed minimal change disease". In SLE patients, up to 90% of people, according to estimates had pathologic findings in respect to renal involvement. Clinically severe nephritis will not appear on biopsy but will develop in only 50% of cases. Subclinical hematuria and/or proteinuria, frank nephrotic syndrome, and rapidly progressing glomerulonephritis with renal function loss are all possible clinical manifestations of lupus nephritis [3]. Generally, lupus nephritis appears within the first five years of the illness, though there are some outliers [15].A total of 66% renal biopsy samples in SLE shown to have tubulointerstitial disease, which is identified by polymorphonuclear leukocytes infiltrates, tubular destruction, and interstitial fibrosis. A poor long-term renal prognosis is strongly predicted by the involvement of tubulointerstitial disease[16,17].I.V pulse glucocorticoid therapy followed by maintenanace of 7.5mg prednisolone/day with immunosuppressives gives a better remission in lupus nephritis. In combination with MMF, calcineurin inhibitors can be given for refractory lupus nephritis[3].(Case-4)"The prevalence of Sjogren's syndrome in SLE patients was 14% to 17.8% in a meta-analysis" by *Yao Q et al [18]*.Sjogren's syndrome is an autoimmune chronic inflammatory disease that mostly affects the lacrimal and salivary glands, causing a reduction in the flow of saliva and tears and, as a result, symptoms of dry mouth and dry eyes. It is further classified into primary and secondary Sjogren's syndrome. Of all causes, rheumatoid arthritis (RA) and SLE are the commonest causes of secondary Sjogren syndrome.(case-5) *Pasoto SG et al- [20]*in their analysis said that around 50-60% lung involvement like pleural effusion, pleuritis, lupus pneumonitis, pulmonary hypertension and diffuse alveolar heamorrhage(DAH) is seen in severe sle cases. DAH is seen in <2% cases in SLE. So DAH is a rare and life threatening manifestation of SLE[19].

CONCLUSION

SLE is a multifactorial auto-immune disease and always it is not necessary to present with a typical malar rash with photosensitivity reactions. Patient can present with various rare presentations as their initial symptoms. This case series has highlighted about the different case presentations and management. Hence irrespective of gender and age all other criterias, clinical examinations and high index of suspicion has led us to the diagnosis of SLE. Patients presenting with any vague symptoms like fever, arthritis, rashes, altered sensorium without a diagnostic clue, definitely an auto-immune panel has to be investigated and connective tissue disorders has to be ruled out.

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DECLARATION

The authors certify that appropriate patient consent and Department consent was obtained for the above publications.

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