Lupus (SlE / Drug induced / Neonatal)

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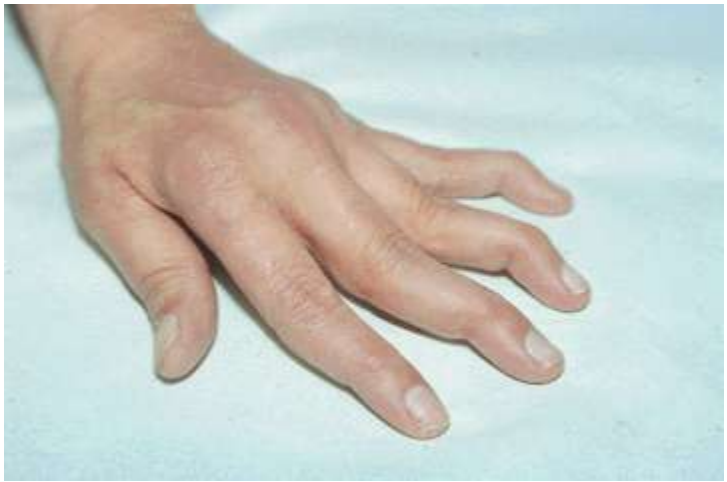
PATHOLOGY & CAUSES

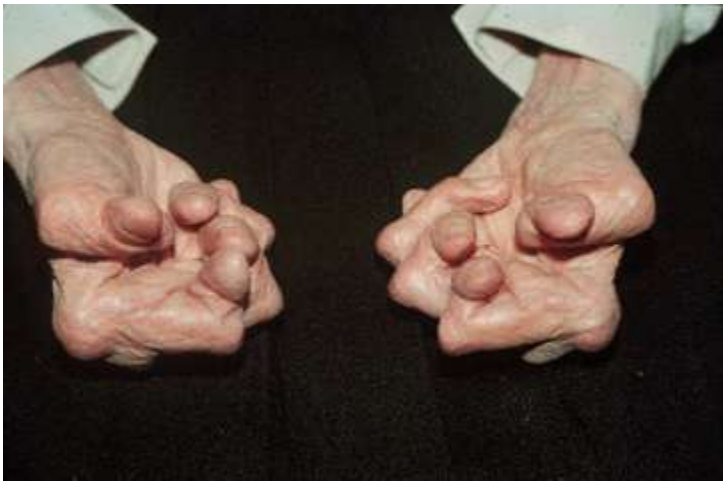
▪ Chronic systemic autoimmune disorder, wide range of clinical, serological features
▪ Periods of flare-ups, remittance
▪ Environmental triggers damage DNA → apoptosis → release of nuclear bodies
▪ Clearance of apoptotic bodies ineffective due to genetic defects → increased amount of nuclear antigens in bloodstream → initiates immune response → production of antinuclear antibodies → bind to antigens, form immune complexes
▪ Complexes deposit in tissues (e.g. kidneys, skin, joints, heart) → Type III hypersensitivity reaction
▪ Individuals may develop antibodies targeting molecules (e.g., phospholipids) of red, white blood cells → marking them for phagocytosis → Type II hypersensitivity reaction → “Penias”!!!

Risk factors : Mix of genetic and hormones and environment
Example : estrogen (3:1 / 12:1 / 8:1 for group age under 14 , 15 to 45 , about 45 respectively)
Or genetics like xxy syndrome (klinefelter syndrome) or xo syndrome

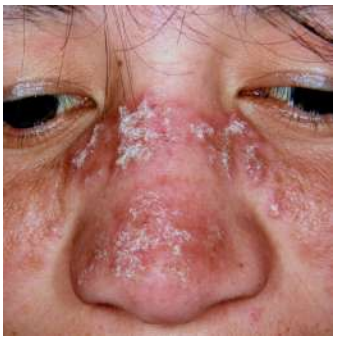
Lab tests : ANA , anti ds-dna - anti smith - anti phospholipid antibody
Low c3 & c4 & ch50
ENA Panel

1. **Constitutional symptoms :** fatigue(80-100%) , fever(50) , weight loss , myalgia
2. **Arthritis and arthralgias :** earliest manifestation , occurs in 65 to 70 percent of patients and tends to be migratory, polyarticular, and symmetrical

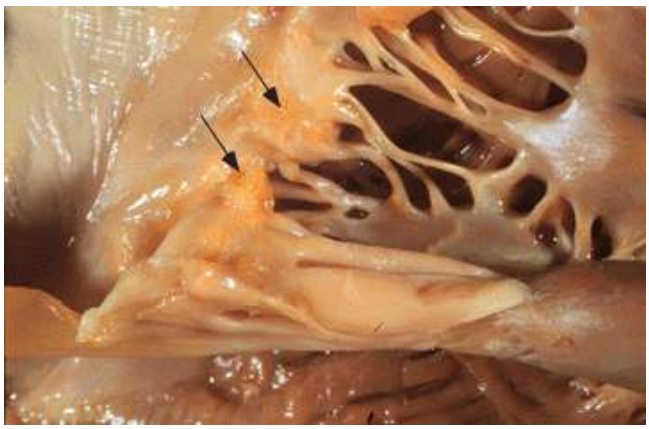


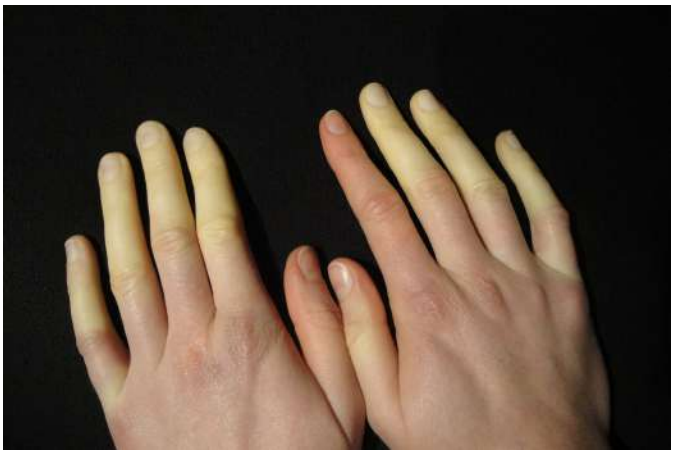


3. **Mucocutaneous involvement :** malar rash , discoid rash , photosensitivity , oral/nasal ulcer



4. **Cardiac involvement and vascular manifestations :** Pericarditis is most common , libman sack endocarditis / heart block in neonatal / Raynaud / Vasculitis / thromboembolic (Anti PLS, Antimalarial drugs)





5. **Kidney involvement :** from asymptomatic to nephritis (DPGN)

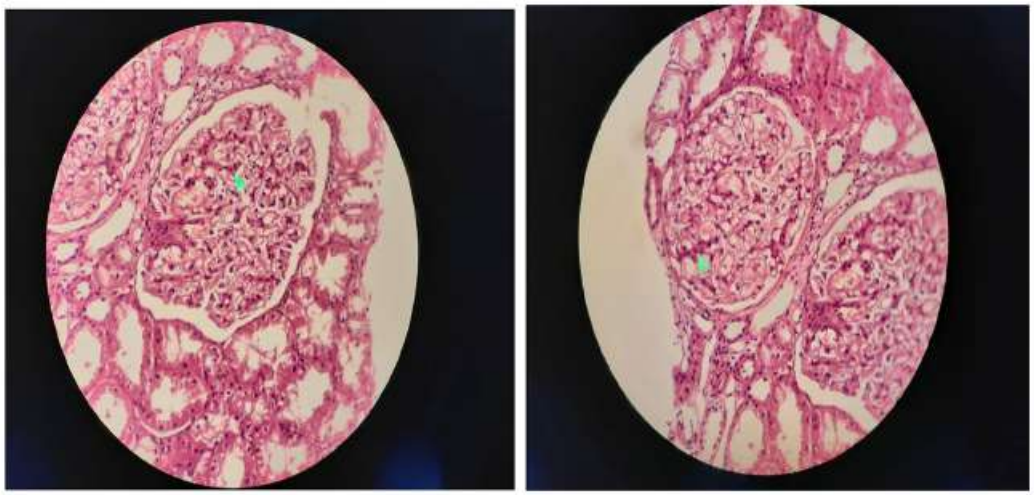


Fig. 2 The histopathology of kidney biopsy in the patient with SLE and COVID-19. Arrow shows inflammatory cell infiltration. A mild mesangial hypercellularity and mild fibrosis is seen in the background

6. **Gastrointestinal involvement**
7. **Pulmonary involvement :** (pleuritis (with or without effusion), pneumonitis, interstitial lung disease, pulmonary hypertension, shrinking lung syndrome, and alveolar hemorrhage)
8. **Neurologic and neuropsychiatric involvement** : seizures, cognitive dysfunction , Memory loss
9. **Hematologic abnormalities :** Anemia , Leukopenia , thrombocytopenia , …

Classification Criterias : 1. Old one (1997) , most recent (2019)

AntiPhospholipid Antibodies:

1. Anti phospholipid syndrome
2. Venous and atrial thrombosis
3. DVT , stroke , Fetal loss

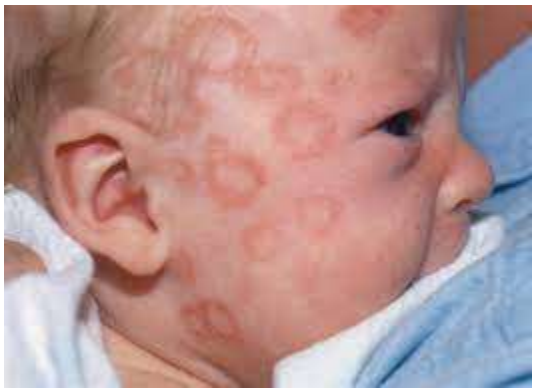
Fasle ptt (lupus anticoagulant) / false syphilis (anti cardiolipin)

Drug Induced lupus :

INH, Procainamid, Minocycline, hydralazine , Anti TNF a
Rashes , arthritis , ANA + , penias
Anti histon antibody

Neonatal lupus :

Sjogren syndrome , Rashes , complete heart block



MEDICATIONS

- **Long term therapy**
  - Antimalarial agents
- **Mild to moderate manifestations**
  - Non-steroidal anti-inflammatory drugs
(NSAIDs), low doses of corticosteroids
- **Severe/life-threatening manifestations**
  - High doses of corticosteroids, intensive immunosuppressive drugs

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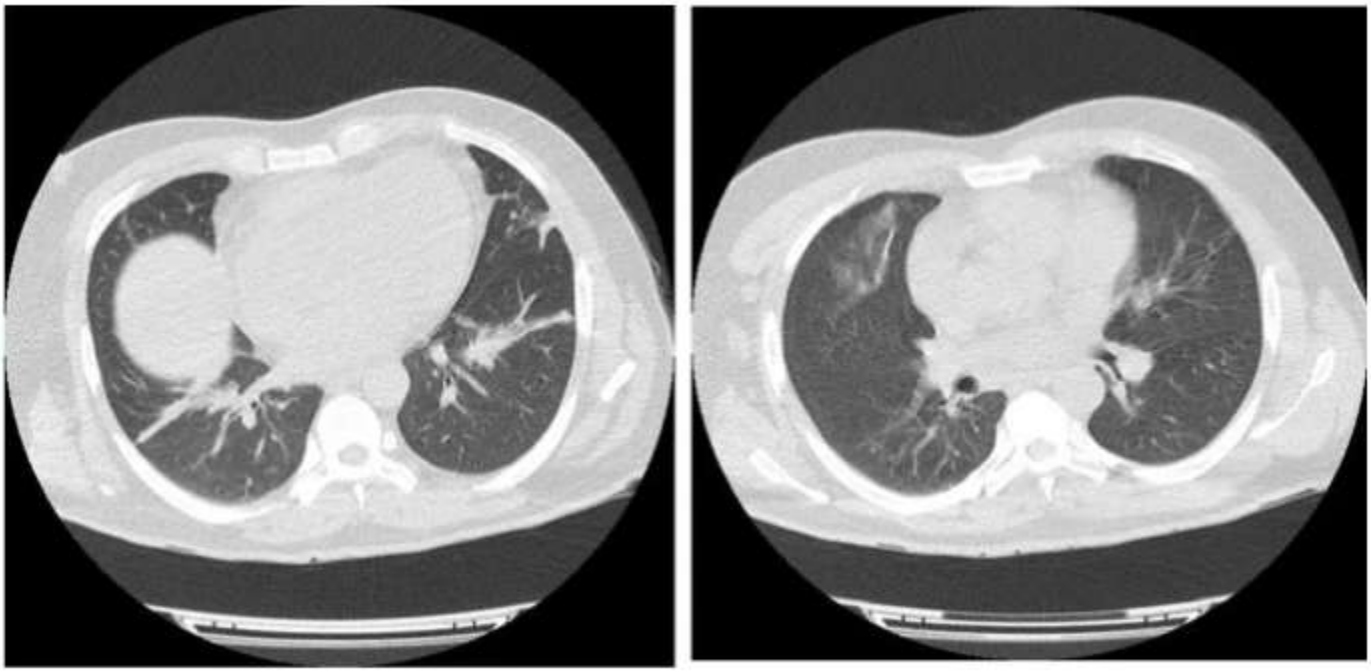
Case Study

A 39-year-old Iranian/Persian man with complaints of fever (38 °C), scaling on the palms of the hands and feet, lower extremity edema, and ankle swelling was referred to Kashan Rheumatology Clinic in 2020.

2 months ago, the patient was referred with complaints of fever, dry cough, shortness of breath, and wheezing. Upon arrival he had a high temperature (38 ℃), a respiratory rate of 22 breaths per minute, a heart rate of 110/min, a blood pressure of 100/70 and oxygen saturation of 93%. The patient had no history of alcohol consumption and cigarette smoking. The result of laboratory tests showed leukopenia (white blood cell (WBC): 4200/mm_3), thrombocytopenia (platelet count: 73,000/mm_3), high C-reactive protein (CRP: 43 mg/L), hemoglobinemia (hemoglobin level: 11.2 g/dL), and normal liver function tests.

Computed tomography (CT) of the chest showed two ground-glass opacity nodules in the lower lobes of both lungs (Fig. 1). SARS-CoV-2 was detected in the nasal swab by reverse-transcription polymerase chain reaction test (RT-PCR). The patient did not need intensive care unit (ICU) admission and underwent outpatient treatment for COVID-19. He was treated with 400 mg oral dose of hydroxychloroquine twice on the first day and 200 mg twice daily for an additional 6 days.

Fig. 1



Chest computed tomography images of the patient with COVID-19. Ground-glass opacity nodules are seen in the lower lobes of both lungs

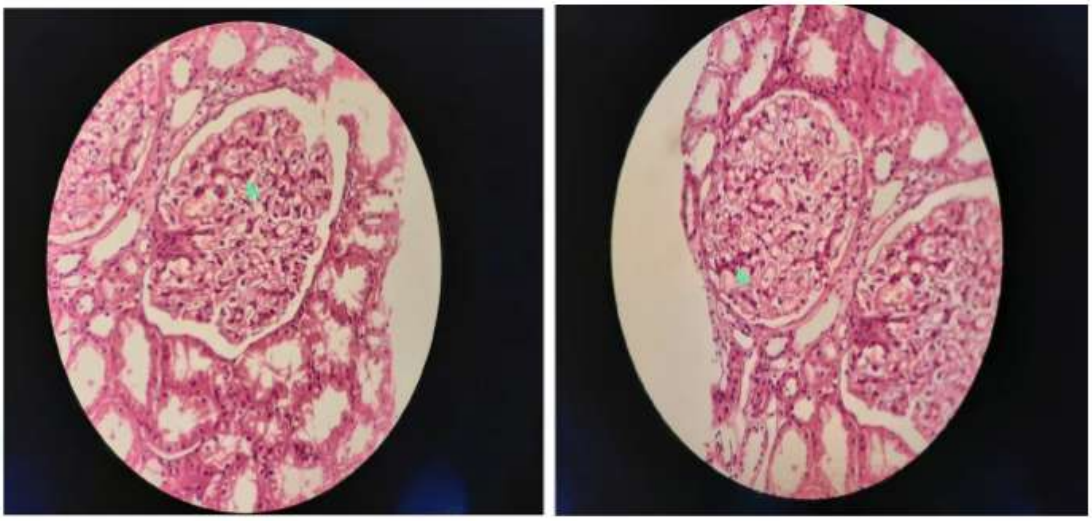
The patient recovered after 4 weeks, but gradually, urticaria-like skin lesions and erythematous rashes appeared on the chest, upper and lower limbs with itching. The patient developed scaling on the palms of the hands and feet and hyperkeratosis of the soles of the feet. Lower extremity

edema and ankle swelling were also added to the complications of the disease. The patient suffered from a weight loss of about 15 kg, anorexia, and headache during 2 months. He was suffering from hyperesthesia of lower extremity on both sides when referred to the rheumatology clinic. He felt severe burning and pain when his feet were touched. The tendon reflexes and strength of the lower and upper limbs were normal. The results of primary laboratory tests were as follows: platelet count, 73,000/mm_3 (150,000–400,000/mm_3); white blood cell count, 4200/mm_3 (4500–11,000/mm_3); (14–18 g/dL); C-reactive protein (CRP) level, 34 mg/L (< 10 mg/L); erythrocyte sedimentation rate (ESR), 74 mm/hour (0–20 mm/hour); lactate dehydrogenase (LDH), 437 U/L (150–450 U/L); troponin I, 3 μg/L (< 0.03 μg/L). Electrolytes, kidney and liver function tests were normal.

Due to the observation of bicytopenia, the patient's peripheral blood smear (PBS) was evaluated by a hematologist. Toxic granulation was observed in the PBS while blast cells and schistocytes were not seen. Patient had a normal echocardiogram. SARS-CoV-2 genome was not detected by RT-PCR. IgG antibodies against SARS-CoV-2 were detectable by the enzyme-linked immunosorbent assay (ELISA) (Pishtaz Teb Zaman, Tehran, Iran), but IgM antibodies against SARS-CoV-2 were negative (Pishtaz Teb Zaman, Tehran, Iran) in the serum sample. Urine analysis showed 2+ proteinuria and 550 mg of protein was measured in the 24-h urine sample. Electromyography (EMG) and nerve conduction velocity (NCV) showed motor and sensory polyneuropathies.

The patient was suspected of having SLE. The results of laboratory tests to diagnosis systemic lupus erythematosus are as follows: total complement activity (CH50), 45 (50–150); complement C3 protein, 133 mg/dL (90–180 mg/dL); complement C4 protein, 14 mg/dL (10–40 mg/dL); anti-La/SSB antibodies, 160 U/ml (< 12 U/mL); anti-SSA/Ro, 200 U/mL (< 25 U/mL); anti-cyclic citrullinated peptides (anti-CCP) antibodies, 48 IU/mL (< 20 IU/mL) ; anti-double-stranded deoxyribonucleic acid antibody (anti-dsDNA), 70 IU/mL (< 35 IU/mL); fluorescence antinuclear antibody (FANA), 1/160. Anticardiolipin, lupus anticoagulant, anti-beta-2 glycoprotein 1, and anti-neutrophil cytoplasmic antibodies (C-ANCA, P-ANCA) were negative. The patient’s kidney biopsy showed a mild mesangial hypercellularity (lupus nephritis class I). Mild intermediate fibrosis was observed in trichrome staining of tissue (Fig. 2).

Fig. 2



The histopathology of kidney biopsy in the patient with SLE and COVID-19. Arrow shows inflammatory cell infiltration. A mild mesangial hypercellularity and mild fibrosis is seen in the background

The treatment with pulse methylprednisolone (1000 mg for three consecutive days) was started and continued with hydroxychloroquine and prednisolone (30 mg daily). Platelets were reduced to 100,000/mm_3 and hemoglobin to 11 g/dL, but paresthesia, proteinuria, and edema continued. The patient has received monthly pulse doses of 1000-mg IV cyclophosphamide. The patient was discharged while being given hydroxychloroquine, prednisolone (10 mg daily), cyclophosphamide, gabapentin, and vitamin B (300 mg daily).

The patient was followed up after the 6-month. Paresthesia was improved. The laboratory tests (CBC, ESR, CRP, T3, T4) were normal and urine protein was 230 mg/daily.
Anti-double-stranded DNA antibody reduced to the normal range (< 35 IU/mL).

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