Case Report

Coronavirus disease-19 triggered systemic lupus erythematous: A novel entity

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ABSTRACT

Coronavirus disease 19 (COVID-19) has been associated with varied immunological diseases due to dysregulated immune responses. We hereby report a rare case of COVID-19 triggered Systemic lupus erythematous arising in a young healthy male, necessitating the use of immunomodulatory drugs for the remission of the disease process.

KEY WORDS: Autoimmunity, coronavirus triggered, COVID-19, lupus erythematous

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INTRODUCTION

Coronavirus diseases officially named COVID-19 by WHO is the disease caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-Cov-2).[1]

It has its origin in Wuhan, Huwai Province, China, on December 19. SARS-CoV-2 belongs to the same genera of beta coronaviruses causing respiratory illnesses in humans such as Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome.[2]

Mortality rates in COVID-19 disease have been documented to be 3.6% in various studies.[3] It has been postulated that one of the factor leading to mortality could be the SARS-Cov-2 associated triggering of rapid autoimmune response resulting in refractory severe interstitial pneumonia in genetically predisposed individuals.[4] Many infectious agents including viral infections are known to be responsible for the initiation or exacerbation of autoimmune diseases.[5] Amongst all the viruses contributing to the aetiology of autoimmune disease, the most compelling evidence has been documented between Epstein bar Virus and Systemic lupus Erythematous (SLE).[6] We hereby describe a microbiologically proven case of COVID-19 Disease, which resulted in the triggering of SLE in a previously healthy young male without any comorbidities.

CASE SUMMARY

A 28-year-old male with no previous comorbidities and no interstate travel history was admitted with complaints of fever, dry cough and breathlessness on exertion for a duration of 3 days. General physical examination of the patient was normal except fever of 100°F. He was maintaining saturation of 95% on room air at rest and post exercise, there was no dip in saturation.

A nasopharyngeal and throat swab was taken for SARS-COV-2 and it tested positive. Hematological parameters showed pancytopenia with a Total Leucocyte Count of 3800/mm^3, Hemoglobin of 9 gm% and mild thrombocytopenia of 1,30,000/mm^3. Chest Radiograph was

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normal. Electrocardiography was normal sinus rhythm with QTc interval of 380 ms. He was diagnosed with Coronavirus disease 19 (COVID-19). His fever subsided after 5 days of symptomatic treatment.

However, after 3 days of an afebrile period, he again started mounting fever. There was a generalised erythematous rash with papules over the extremities and face along with mucosal involvement [Figure 1a]. Oral mucosa was involved in the form of painless ulcers. Work up for fever including Dengue Ns1Ag, Dengue serology and Blood for Malarial Parasite was negative. Serology for Scrub Typhus and Leptospira was negative. Urine Routine and microscopic examination were normal. Blood culture and urine culture showed no growth. His repeat nasal and throat swab test for SARS-COV-2 was negative. Viral markers including HIV, HBsAg and Hepatitis C were negative. CRP levels were 25 mg/L and IL6 levels were 15 pg/mL.

His pattern of fever was continuous in nature with a maximum spike of 102.8°F. He underwent CECT Chest and Abdomen to look for secondary infections. It revealed Ground glass haziness involving bilateral lower lobes and patchy areas of consolidation involving bilateral upper lobes [Figure 2a, b]. Sputum examination for Gram stain, Acid Fast Bacilli, and Fungal stains were negative. Sputum culture for bacteria and fungi yielded no growth. He was empirically treated with broad spectrum intravenous antibiotics and it was de-escalated as serum procalcitonin levels were normal. During examination, lymph node enlargement was found in axillary and cervical regions. Lymphadenopathy was soft, non-tender, discrete and non-matted. In view of pancytopenia and persistence of fever, he was worked up for Secondary hemophagocytic lymphhistiocytosis (sHLH). Levels of Serum ferritin and Serum triglyceride were 680 ng/ml and 118 mg/dl, respectively.

Bone marrow examination showed reactive marrow without any features of hemophagocytosis. No granulomas or blast cells were seen. He underwent a Fine needle aspiration of the Cervical lymph node. It tested negative for GeneXpert MTB. Cervical lymph node biopsy showed follicular hyperplasia with no evidence of granuloma/malignancy and no features of hemophagocytosis. Based on the HS score probability of him suffering from HLH was less than <1%.[7]

As a part of the work up for PUO, testing of Antinuclear antibody (ANA), Rheumatoid arthritis (RA) factor was done. ANA titres by Enzyme immunoassay (EIA) were significantly high 208.79 units (>60: Strongly positive). RA factor was negative. Extractable nuclear antigen antibody profile by EIA showed positivity to Smith (Sm), anti-double standard DNA. C3 and C4 complement levels were low. Immunological work up at tertiary care center revealed positive ANA by Indirect immunofluorescence (IIF) method (4+ Speckled). Based on EULAR 2019 criteria, he was diagnosed to be suffering from SLE, triggered by COVID-19. He was started on a daily dose of Tab HCQS 300 mg once daily (OD), Tab Prednisolone 10 mg OD and Tab Azathioprine 75 mg OD. He showed a favourable response to treatment. Fever subsided and skin rash resolved [Figure 1b]. Repeat CECT Chest showed normal scan with complete resolution of ground glass haziness [Figure 2c, d] and there was a significant decrease in cervical and axillary lymph nodes. His pancytopenia resolved and weakness subsided. During follow-up visit at the completion of 1 year, ANA positivity was persistent by IIF and he was asymptomatic on immunomodulatory therapy.

DISCUSSION

Various causative factors play a role in the development of autoimmune diseases in a host which includes genetic predisposition and precipitating factors consisting of infections, environmental agents and hormonal factors. The interplay of all these factors leading to autoimmune diseases

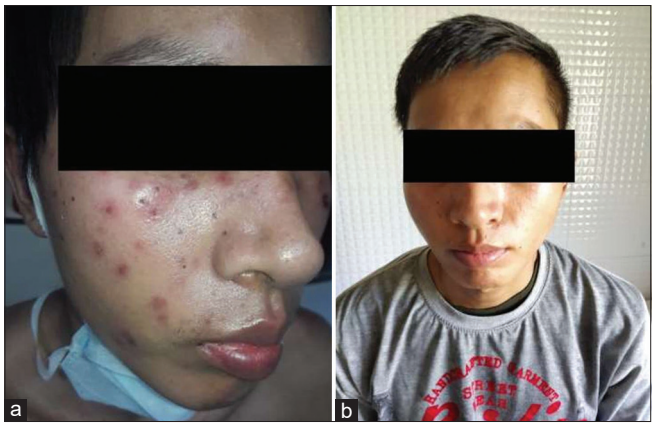

Figure 1: (a) Erythematous rash with papules involving the face. (b) Post Treatment: Complete resolution of rash comparing with Figure 1a.

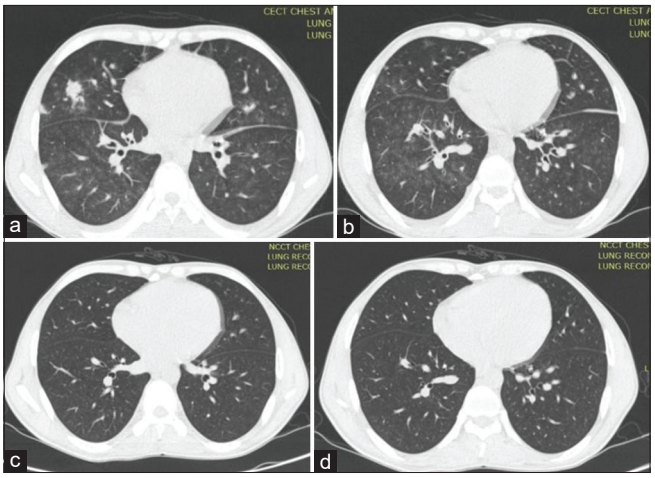

Figure 2: NCCT Chest showed (a) Patchy areas of consolidation involving posterior segments of right upper lobe and left upper lobe. (b) Ground Glass haziness involving bilateral lower lobes. (c) Complete resolution of patchy consolidation involving bilateral upper lobes comparing with Figure 2a. (d) Resolution of ground glass haziness involving bilateral lower lobes, which was evident in Figure 2b.

has been coined as 'The Mosaic of autoimmunity'.[8] Viruses play a predominant role amongst all the environmental factors in the activation of autoimmune diseases through various mechanisms including molecular mimicry, bystander activation and epitope spreading.[9] COVID-19 since its inception has been linked to various immunological diseases ranging from Immune thrombocytopenic purpura, Guillian Barre Syndrome, Antiphospholipid syndrome and Kawasaki-like disease.[10] Cytokine storm syndromes including the HLH are the most dreaded autoinflammatory response associated with COVID-19.[10] sHLH is a type of cytokine storm syndrome which may present with fever as an initial manifestation and prompt the work-up in our patient. Based on Hscore developed by Fardet *et al*.,[7] our patient had a total point of 99, which corresponds to around 1% probability of hemophagocytic syndrome. A strong association of COVID-19 with sHLH prompted work-up for it in our patient, which turned out to be negative. ANA levels were done as part of work-up for PUO amid pancytopenia, rash and lymphadenopathy. EULAR/ACR criteria 2019 having a sensitivity of 96% and specificity of 93.4% were adopted to diagnose SLE.[11] ANA titre ≥1:80 is the obligatory criterion. In addition to this, 07 clinical domains and 03 immunological domains were added. These clinical and immunological domains were given a point weightage from 2 to 10. Out of the 07 clinical domains described, our patient fulfilled criteria from constitutional, hematological and mucocutaneous domains. From the 03 Immunological domains, our patient satisfied 02 domains. Taking account of all scores, our patient had obligatory criteria, one clinical criteria and total score more than 10. He was diagnosed as SLE and was treated accordingly. In our case, COVID-19 triggered SLE, which may have been lying in the quiescent phase. Our case emphasises the important role played by SARS-COV-2 in activating the immune-inflammatory pathways leading to autoimmune diseases in genetically predisposed individuals. It also emphasizes the need for work-up for autoimmune diseases in cases of Pyrexia of unknown origin.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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