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Case Report

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COVID-19 infection may trigger SLE disease: A case report

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Abstract

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect various body organs, especially the skin, joints, hematopoietic system, kidneys and central nervous system. The signs and symptoms occur depending on the inflammation in the affected tissues. Although many factors are responsible for its aetiology, it is known that some viruses such as Epstein Bar virus may also cause this disease by triggering autoimmunity. Recent studies have revealed that the immune system could be activated due to coronavirus infections and that some autoantibodies could be observed in the blood. A small number of SLE cases activated by COVID infection have been reported in the literature. The present study presented and discussed with the information in the literature a 20-year-old patient with COVID infection, diagnosed with SLE with renal involvement according to EULAR/ACR 2019 criteria by considering histopathological and immunofluorescence findings.

Keywords: lupus erythematosus, systemic, COVID-19, antibodies, autoimmune diseases

1. Introduction

COVID-19 disease, which primarily affects the respiratory system, can manifest itself with various clinical findings ranging from being an asymptomatic carrier to multiorgan failure. After the World Health Organization declared the COVID-19 outbreak a pandemic, no effective treatment for the disease has been found so far. The virus undergoing mutation over time can manifest in a wide range of clinical presentations. Besides the virulence, co-morbidities and immune response are known to be effective in the severity of the clinical state (1, 2). Activation of the immune system and some autoantibodies has been shown in COVID-19 patients (3,4). Additionally, the corrective effect of immunosuppressive treatment on the clinical state has been reported for some critical COVID-19 patients (5). Causes triggering autoimmunity may play a role in the development of SLE. Accordingly, the possibility of COVID-19 disease triggering autoimmunity and playing a role in SLE development can be considered. The literature reported 4 SLE cases triggered by COVID-19 infection (6-9). The present study discussed a recently diagnosed SLE patient with renal involvement and COVID infection. Ours is the first case whose diagnosis was confirmed with immunofluorescence microscopy.

2. Case report

A 20-year-old patient, who was 22-weeks pregnant, applied at the emergency room with complaints of 2-weeks of edema in the lower extremity, knee pain and extensive muscle pain. The patient's health history revealed this to be her first pregnancy, and she had no chronic disease, substance or alcohol use or complaints such as cough, fever, shortness of breath. Her examination findings and blood tests (including urea and creatinine) had been normal in the 12-week routine prenatal visit. We detected pretibial edema in both lower limbs in her examination in the emergency room. Her knee motions were painful, and we found no effusion or redness in the joints. The laboratory investigations showed the following results: creatinine value: 2.49 mg/dl (0.5-1.1), urea: 139 mg/dl (19-49) Na: 131 mEq/L (132-146), potassium: mEq/L6.4 (3.5-5.5) CRP 3 mg/L(0-5) sedimentation rate: 45 mm/h, WBC: 10750 x 109/L, PLT:146000 x 109/L, Hb: 11.8 g/dL, Total protein: 43 gr/l (57-82), Albumin: 20 gr/l(32-48), Uric acid: 10.3 mg/dl(3.1-7.8), Spot urine protein/creatinine ratio: 1387 (200<), Urinalysis proteinuria (4+ protein>), 175 Red blood cells/ high-power field (HPF) , 46 leukocytes/HPF, 3 leucocyte clusters.

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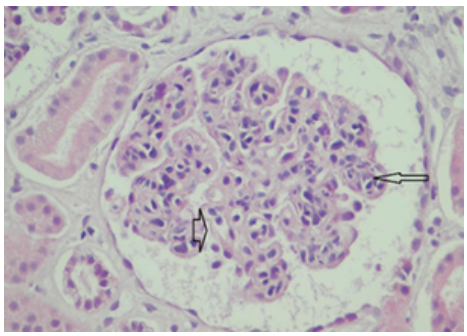

Fig. 1. Thickening in the glomerular tuft and in the glomerular basement membrane, double contour (thick arrow), mesangial cell and matrix increase (long arrow) (H&Ex400).

We detected 24-hour urine output of 150 ml. E. Coli grew in urine culture. We gave intravenous Ertapenem to treat the urinary tract infection. Immunologic test results showed signs of autoimmune disease, including 1:3200 positive antinuclear antibodies (ANA) with a coarse speckled pattern. Anti-ds DNA-ELISA: 460 RU/ml (<100), Anti SS-A: 3+, Anti Ro-52:3+, Anti SS-B: 3+, Nucleosome: 2+, Anti-histone: 3+, Anti-glomerular basement membrane antibody (Anti GMB): negative, Antiphospholipid antibodies: negative, C3c g/L:0.2 (0.9-1.8), C4 g/L: 0.1 (0.1-0.4), MPO ANCA-ELISA: Negative, PR3 ANCA-ELISA negative, P ANCA – ELISA negative, C ANCA-ELISA negative. COVID reverse transcription-polymerase chain reaction (RT-PCR) with a nasopharyngeal swab and COVID-19 IgG+IgM antibody were positive 4.12 (0-0.99). Serology tests results for other viruses were the following: Anti EBV IgM: negative, Anti EBV IgG: negative, Anti-Toxoplasma IgM: negative, Anti-Toxoplasma: IgG negative, Antirubella Ig M: negative, Antirubella IG G: positive, Anti CMV IgM: negative, AntiCMV Ig G: positive, Parvovirus IgM: negative, Parvovirus IgG positive. We detected Grade 1 increase in the parenchymal echogenicity in kidney ultrasound. Meanwhile, the patient's pregnancy ended due to intrauterine fetal death. We performed an ultrasound-guided kidney biopsy for histopathological examination and observed 40 glomeruli and seven arteries in the sections taken. Histopathological findings of kidney tissue revealed thickening of the basement membranes, double contour formation, mesangial cell and matrix increase in more than 50% of the glomeruli, with more prominence in general in the peripheral capillary loops (Fig. 1). We observed inflammatory cell infiltration containing a mild level of lymphocytes in the interstitium and degenerative and regenerative changes in tubular epithelial cells. We also observed thickening in the glomerular basement membrane with PAS-Methanomine Silver and PAS and staining in the immunofluorescence sections with IgG, IgM, C1Q, IgA, C3; C4c; Kappa, lambda (Fig. 2). but no staining with fibrin or albumin. Histopathological and immunofluorescence findings were consistent with diffuse proliferative glomerulonephritis (full house nephropathy) and evaluated as Class 4 lupus nephritis. We diagnosed the patient with SLE according to the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) 2019 criteria (10), gave Methylprednisolone 1gr/day for three days and maintenance steroid treatment after that and started cyclophosphamide to be administered 750 mg once every three weeks. We obtained informed consent from the patient.

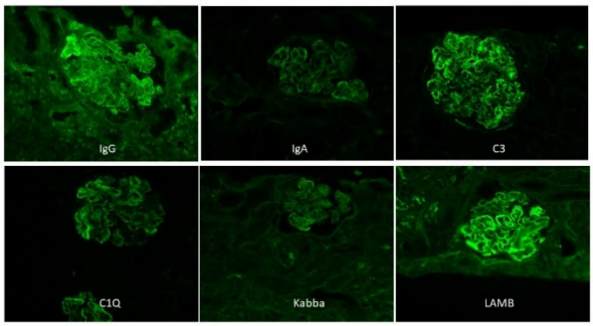

Fig. 2. In immunofluorescence staining, staining is present in the subendothelial area in the glomerular tuft: + 3 with IgG(a), C3c(d), Lambda(g), +2 with C1q(e), +1 with IgM(b), IgA(c), Kappa(f).

3. Discussion

SLE is an inflammatory disease in which autoimmunity, triggered by genetic environmental factors, plays a role in its aetiology, seen more frequently in females (11). Smoking, alcohol use, ultraviolet radiation exposure, vaccines, silica exposure, air pollution and solvent exposure can be counted among the environmental factors triggering SLE development (11,12). Besides these, it has been reported that infectious diseases such as Epstein-Barr virus (EBV) and cytomegalovirus could trigger SLE development (11,13,14).

After the COVID-19 pandemic, newly diagnosed SLE cases triggered by its infection have been reported (6,7,8). The key role of autoimmunity in the etiopathogenesis of SLE and activation of the autoimmune system by COVID-19 disease seem to be the two factors responsible for this relationship. Wang Y et al. detected SARS-CoV-IgG and -IgM antibodies in the serums of %3 of 114 healthy individuals without COVID-19 disease and 32% of 58 SLE patients (15). Another study found SARS-CoV-IgG positivity with a rate of 3% in 66 healthy individuals and 58% SARS-CoV-IgG positivity and 29% SARS-CoV-IgM positivity in 31 SLE patients, while the PT-PCR test was negative for all these patients (16). According to the authors, one possible reason for the false-positive results of SARS-CoV-IgG and IgM antibody in SLE patients is the antigens coated with SARS-CoV and Vero-E6 cells in ELISA methods (16). Because SARS-CoV antibodies cannot be detected in the early stage of the coronavirus disease, an ELISA test 2-3 weeks after the onset of the symptoms is recommended (16,17). In our case, the patient's PT-PCR test was positive when she applied at the hospital. We detected antibodies in her blood one week later with the ELISA test. The positivity of her PT-PCR test suggested that these antibodies were related to COVID-19. Zhou Y et al. reported that they found anti-52 kDa SSA/Ro antibody/25 and anti-60 kDa SSA/Ro antibody in 20% and ANA positivity in 50% of 21 critical

COVID-19 patients. They also reported that autoimmune pneumonia developed in 3 patients (3). The authors have interpreted this situation as a sign of the deterioration of the immune functions in COVID-19 patients. Similarly, we also detected ANA and anti-52 kDa SSA/Ro antibody positivity in our SLE patient with COVID-19, besides anti ds DNA, Anti SS-A, Anti SS-B, Nucleosome and Anti Histone positivity.

In our case, the coexistence of newly developed SLE disease and COVID-19 may be coincidental. However, the involvement of viruses such as EBV in the etiology of SLE, (13) immune system activation, of which the presence is well-known in COVID-19 disease, (1) and the common antibody that can be found in both diseases (3) demonstrated that COVID-19 infection might trigger SLE disease. Prospective controlled studies are needed to determine whether COVID-19 infection plays a role in the etiology of SLE or other autoimmune diseases.

Conflict of interest

The authors declared no conflict of interest.

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None to declare.

Authors' contributions

Concept: Y.M., Design: E.A., Data Collection or Processing: N.S., Ş.K.C., Analysis or Interpretation: M.K., B.P., Literature Search: B.P., Writing: EA., M.K.

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