OLGU SUNUMU CASE REPORT

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A Case Report with Post COVID-19 Lupus-Pernio-Like Syndrome

COVID-19 Sonrası Lupus-Pernio-Benzeri Sendromlu Bir Olgu Sunumu

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ÖZET Koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)], çeşitli diğer virüslerde gördüğümüz gibi çeşitli otoimmün hastalıkları tetikleyebilir. Bunlara örnek olarak Guillain-Barré sendromu, Bell paralizi, Miller Fisher sendromu ve hastalığa bağlı viral artrit verilebilir. COVID-19 pandemisi tüm dünyada hızla ilerlerken bu alandaki literatür bilgimiz de hızla artıyor. Burada COVID-19 sonrası lupus-pernio-benzeri sendrom tanısı konan 30 yaşında bir kadın hastayı sunuyoruz. Hasta, sağ ayak bileğinde şişlik ve sıcaklık, sağ elin 5. parmağında (küçük parmak) ağrı ve şişlik şikâyetleri ile tarafımıza başvurdu. Öz geçmişinde 2 ay önce COVID-19 geçirdiği öğrenildi. Hasta nonsteroid antiinflamatuar tedaviden fayda görmedi. Güncel literatürde COVID-19 sonrası ilişkili lupus-pernio-benzeri sendromu olan birkaç olgu bildirilmiştir.

Anahtar Kelimeler: COVID-19; lupus pernio; artrit

ABSTRACT Coronavirus disease-2019 (COVID-19) can trigger a variety of autoimmune diseases, as we have seen with a variety of other viruses. Examples of these are Guillain-Barré syndrome, Bell's palsy, Miller Fisher syndrome and viral arthritis related to the disease. The COVID-19 pandemic is progressing rapidly all over the world, our literature knowledge in this field is rapidly increasing. Here, we present a 30-year-old female patient diagnosed with post-COVID-19 lupus-pernio-like syndrome. The patient presented with the complaints of swelling and warmth in the right ankle and pain and swelling in the 5th finger (little finger) of the right hand. In her history, it was learned that she had COVID-19 2 months ago. The patient did not benefit from the non-steroidal anti-inflammatory treatment. A few cases with post-COVID-19 associated lupus-pernio-like syndrome have been reported in the current literature.

Keywords: COVID-19; lupus pernio; arthritis

While the coronavirus disease-2019 (COVID-19) pandemic is progressing rapidly all over the world, our literature knowledge in this field is rapidly increasing. Today, we know that the infection causes various clinical symptoms in many systems, mainly the cardiopulmonary system. Dyspnea, pneumonia, cytokine storm and thrombosis complications lead to a fatal course of the infection.

The first target of COVID-19 is the upper respiratory tract mucosa and it acts as a functional receptor for angiotensin-converting enzyme 2 (ACE2) virus. Expression of the COVID-19 cell receptor gene *ACE2* has been demonstrated in a number of human tissues including skin and adipose tissue.[1]

Our literature on COVID-19 related skin findings, arthritis and autoimmune disease is increasing

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day by day.[2,3] Chilblain-like edematous and erythematous eruptions have been observed in COVID-19, which disappear after remission without scars.[2] Researchers have been started to focus on post-COVID-19 immune system effects and alterations.[3] Here, we present a 30-year-old female patient diagnosed with post COVID-19 lupus pernio-like syndrome and whose informed consent was obtained.

CASE REPORT

The patient presented with the complaints of swelling and warmth in the right ankle and pain and swelling in the 5th finger (little finger) of the right hand. In her history, it was learned that she had COVID-19 2 months ago and she survived the treatment with outpatient oral treatments. She stated that after COVID-19, dry mouth, wound in the corner of the mouth and hair loss started. She also stated that after 1.5 months, swelling, pain and throbbing developed firstly in the left ankle and then in the right ankle. She said that the 5th finger on both hands first left and then the right hand swollen and turned purple.

Laboratory parameters were as follows: Leukocyte: 11.7 (neutrophil: 7.2, lymphocyte: 2.9, monocyte: 0.95, eosinophil: 0.51, basophil: 0.04), hemoglobin: 13.5, platelet: 188.000, uric acid: 3.3 (2.4-5.7), antinuclear antibody (immunofluorescence assay): 0.3 (<0.8 negative), activated partial thromboplastin time: 24.8 (20-35), prothrombin time: 12.5 (11-16), international normalized ratio: 1.06 (08-1.2), rheumatoid factor: 21.2 (0-20), C4: 0.214 (0.16-0.38), anti cyclic citrullinated peptide: 0.5 (0-5.00), erythrocyte sedimentation rate: 16 (0-30), C-reactive protein: 8.65 (0-8.00), C3: 1.060 (0.79-1.52), anti dsDNA: negative, anti SS-A: 3.23 (0-12), anti SS-B: 2.57 (0-12), proteinase 3 anti-neutrophil cytoplasmic antibody (ANCA): negative, myeloperoxidase ANCA: negative, ANCA profile: negative, D-dimer: 0.32 (0-0.55), urine test: 1 leukocyte (Table 1).

The patient did not benefit from the non-steroidal anti-inflammatory oral treatment given from the outpatient clinic for 10 days. She did not describe any arthritis or related disease in her past history. It was learned that she did not have a living child with one pregnancy loss. She has no known disease other than iron deficiency anemia.

Angular cheilitis on the left lip of the patient was seen who came to the control physical examination in a wheelchair; there were signs of swelling and bruising of 5th finger in the right hand (Figure 1). There were swelling, pain and warmth in the right ankle. Livedo reticularis was associated with joint swelling in the right hand 5th finger and right toe (Figure 2, Figure 3). The patient was hospitalized with pre-diagnoses of COVID-19 associated chilblain-like acral lesions, lupus pernio, reactive arthritis and antiphospholipid antibody (aPL) syndrome.

In venous Doppler ultrasonography, the diameters of the common femoral vein, deep femoral vein, superficial femoral vein, and popliteal vein were normal and there was no thrombus appearance. There were 2 leukocytes in the urine. Dermatology was consulted due to lesions in the mouth, hair loss and pernio findings.

Prednisolone 16 mg (p.o.), subcutaneous enoxaparin 0.6 cc once daily subcutaneous, and hydroxy-

TABLE 1: Laboratory parameters of the patient.

Leukocyte	11.7
Hemoglobin	13.5
Platelet	188.000
Uric acid	3.3
ANA (IFA)	0.3
Activated partial thromboplastin time	24.8
Prothrombin time	12.5
International normalized ratio	1.06
Rheumatoid factor	21.2
C4	0.214
C3	1.060
Anti cyclic citrullinated peptide	0.5
Erythrocyte sedimentation rate	16
C-reactive protein	8.65
D-dimer	0.32
anti dsDNA	Negative
anti SS-A	3.23
anti SS-B	2.57
PR3 ANCA	Negative
MPO ANCA	Negative
ANCA profile	Negative
Urine test	1 leukocyte

ANA (IFA): Antinuclear antibody (immunofluorescence assay); PR3 ANCA: Proteinase 3 anti-neutrophil cytoplasmic antibody; MPO: Myeloperoxidase.

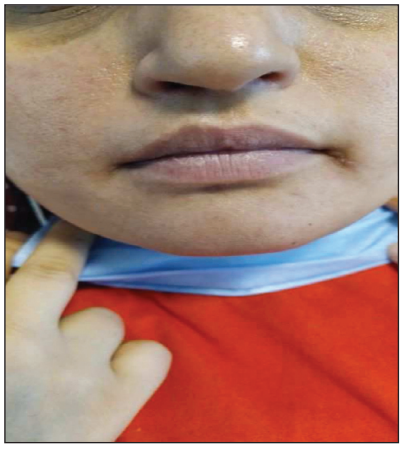

FIGURE 1: Angular cheilitis.

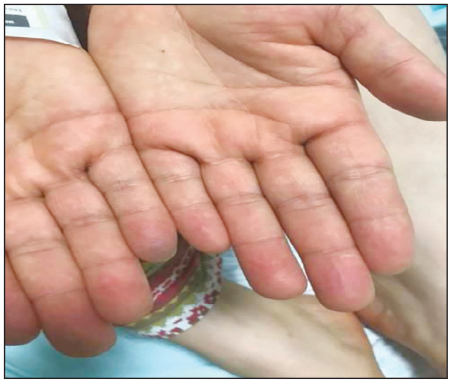

FIGURE 2: Swelling and bruising on the right little finger.

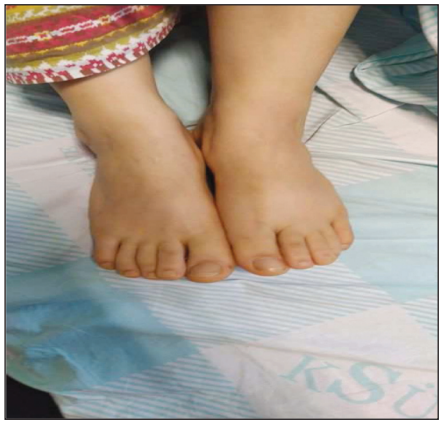

FIGURE 3: Diffuse swelling in the right ankle and livedo reticularis on the right toe.

chloroquine 200 mg bid (p.o) were started. aPL; anticardiolipin (aCL) immunoglobulin (Ig) G was 2.29 (0-12) and IgM were 3.71 (0-12) and anti-β2-glycoprotein (aβ2GP) IgG was 1.15 (0-12) and IgM was 2.3 (0-12). After oral steroid and enoxaparin, the ankle swelling regressed and the heat disappeared. Visual analog scale for pain regressed from 9 cm to 3 cm.

DISCUSSION

COVID-19 pandemic caused by severe acute respiratory syndrome-coronavirus-2 primarily affects the epithelium of the airways. With the increasing involvement of dermatologist in management of this crisis, cutaneous symptoms gained more and more attention. It is known that COVID-19 causes microvascular damage and thrombosis through erythrocyte damage and complement activation, causing skin lesions. The incidence of skin lesions due to COVID-19 was reported to be between 0.2% and 29%. Many skin lesions including maculopapular, urticarial, vesicular, chilblain-like, thrombotic/ischemic, etc. are observed in COVID-19 patients. Chilblain/pernio-like lesions are mostly asymmetrical, painful, edematous, erythematous or purplish plaques in young adults. It has been reported that they regress without scarring in an average of 2 weeks after infection.[3,4]

Although COVID-19 is commonly considered a respiratory disease, there is clearly a thrombotic potential that was not expected. The pathophysiology of the disease and subsequent coagulopathy produce an inflammatory, hypercoagulable, and hypofibrinolytic state.[5] Like previous coronaviruses, COVID-19 seems to cause damage to many organs and tissues through endothelial dysfunction.[6]

In COVID-19 patients, we are faced with an increased risk of thrombosis accompanied by high D-dimer and fibrin degradation products. Zhang et al. described three cases of thrombosis associated with antiphospholipid antibodies represented by anticardiolipin (aCL) and anti-β2 glycoprotein I (aβ2GPI).[7] No lupus anticoagulant (LAC) was detected in the patients. Harzallah et al. examined 50 COVID-19 patients.[8] Twenty five cases (45%) were LAC positive, whereas aCL or aβ2GPI were detected in only five of 50 tested patients (10%).[8]

Antiphospholipid antibody syndrome is characterized by recurrent thrombosis and unexplained

fetal losses. Among antiphospholipid antibodies (aPL), LAC and ACA are especially important.[9,10] High incidence of thrombosis in COVID-19 patients indicates a hypercoagulable state. Hence, exploring the involvement of antiphospholipid antibodies (aPL) in these patients is of interest. Studies have shown that aPL antibodies are temporarily positive and pathogenic in a significant proportion of COVID-19 patients.[11] On the other hand, Devreese et al. observed frequent single LAC positivity during (acute phase) in COVID-19 infection; however, not clearly related to thrombotic complications but related to infection.[12]

COVID-19 can trigger a variety of autoimmune diseases, as we have seen with a variety of other viruses. Examples of these are Guillain Barre syndrome, Bell's palsy, Miller Fisher Syndrome and viral arthritis related to the disease.[13] We found a sufficient number of case reports in the literature that developed systemic lupus erythematosus (SLE)-like clinical pictures due to COVID-19.[14-16] In addition, the Chilblains finding in acquired lupus and interferonopathies are frequently encountered due to COVID-19. Battesti et al. compared the cases of chilblains due to lupus (11 cases) and due to COVID-19 (7 cases) and did not observe any difference in terms of age of occurrence, clinical findings and autoantibodies.[17]

Antiphospholipid antibody syndrome was ruled out with negative antiphospholipid antibodies in a patient with a pregnancy loss. The diagnosis of COVID-19-associated chilblain-like acral lesions was ruled out because the COVID-19 PCR test was negative and there were no findings supporting the disease in the relevant laboratory and imaging tests. The diagnosis of lupus pernio was ruled out because SLE-associated autoantibodies were negative and did not meet the diagnostic criteria. Angular cheilitis on the lip was associated with dry mouth. The emergence of symptoms after 2 months after COVID-19 infection, accompanying arthritis in acral lesions, presence of livedo reticularis, rapid response to steroid-hydroxychloroquine and enoxaparin treatments suggested post COVID-19 lupus pernio-like syndrome.

We see COVID-19 may trigger autoimmune diseases in patients as other viruses did before. A few cases with post-COVID-19 associated lupus-pernio-like syndrome have been reported in the current literature. Our case is compatible with seronegative lupus-pernio-like syndrome started in the post-COVID-19 subacute period in a 30-year old female. It contributes to the current literature.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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