

Urticaria and Angioedema in a Patient Diagnosed with COVID-19: Case Report

COVID-19 Tanısı Olan Bir Hastada Ürtiker ve Anjiyoödem: Olgu Sunumu

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ABSTRACT

Coronavirus disease 2019 (COVID-19) disease caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) virus, which has affected the whole world, can cause clinical pictures ranging from mild cold symptoms to severe lower respiratory tract infections that can cause mortality. Recently, reports of dermatological findings associated with COVID-19 such as urticaria has been increasing. Here, a COVID-19 case presenting with urticaria and angioedema is described. A 26-year-old female patient, who was found to be SARS-CoV-2 positive by polymerase chain reaction performed for being in contact, presented to our outpatient clinic with complaints of itchy, erythematous lesions on her body and swelling in the eyes and throat for four days. The patient received favipiravir treatment for 5 days and these complaints started 4 days after the treatment ended. History of food and other drug allergies, insect bites and chemicals were questioned in the differential diagnosis for etiology, however, no relationship was detected. Systemic corticosteroid and antihistamine treatment was initiated, and edema in the eyes completely regressed and urticaria plaques faded on the 3rd day of the treatment. Dermatological findings may occur simultaneously with the classic symptoms of the disease or before or after symptoms. Although the pathogenesis between dermatological findings and COVID-19 has not been fully elucidated, studies have suggested that viral infections and SARS-CoV-2 can be an etiological agent for chronic or acute urticaria. It is thought that some rashes may be causally related to the viral effect and others to the immune response. It is emphasized that there may be atypical findings such as urticaria/angioedema in order to diagnose COVID-19 disease early and prevent its spread and should be considered in differential diagnosis.

Key Words: COVID-19; Urticaria; Angioedema

ÖZ

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Tüm dünyayı etkisi altına alan Şiddetli Akut Solunum Sendromu Virusu-2 (SARS-CoV-2)'nin neden olduğu yeni koronavirus hastalığı (COVID-19), hafif soğuk algınlığı semptomlarından mortaliteye sebep olabilen ağır alt solunum yolu enfeksiyonlarına kadar değişen klinik tablolara neden olabilmektedir. Son zamanlarda ürtiker gibi COVID-19 ile ilişkili dermatolojik bulguların bildirimi artmaktadır. Burada ürtiker ve anjiyoödem tablosuyla başvuran bir COVID-19 olgusu anlatılmıştır. Temaslı olduğu için yapılan testte SARS-CoV-2 polimeraz zincirleme reaksiyonu pozitif saptanan 26 yaşında bir kadın hasta, dört gündür olan vücudunda kaşıntılı, eritemli lezyonlar, gözlerde ve boğazda şişlik şikayetleri ile polikliniğimize başvurmuştur. Hasta 5 gün süreyle favipiravir tedavisi almış ve tedavisi bittikten 4 gün sonra bu şikayetleri başlamıştır. Hastanın etiyolojik ayırıcı tanısında gıda ve diğer ilaç alerjisi öyküsü, böcek ısırması ve kimyasallar gibi diğer maddeler sorgulanmış ve bir ilişki tespit edilememiştir. Hastaya sistemik kortikosteroid ve antihistaminik tedavisi başlanmış, tedavinin 3. gününde gözlerdeki ödemin tamamen gerilediği, ürtiker plakların solduğu görülmüştür. Dermatolojik bulgular, hastalığın klasik semptomları ile eş zamanlı olarak ortaya çıkabileceği gibi, semptomlardan önce veya sonra da ortaya çıkabilmektedir. Dermatolojik bulgularla COVID-19 arasındaki patogenezi henüz tam olarak aydınlatılmamış olmakla birlikte, yapılan çalışmalarda viral enfeksiyonların ve SARS-CoV-2'nin kronik veya akut ürtiker için bir etiyolojik ajan olabileceği öne sürülmektedir. Bazı döküntülerin doğrudan viral etkiyle, bazılarının ise immün yanıt ile ilişkili olabileceği düşünülmektedir. Tüm dünyada COVID-19 hastalığının etkileri hala devam ederken, hastalığın erken tanınması ve yayılmasının önlenmesi çok önemlidir. Bu sebeple, ürtiker/anjiyoödem gibi atipik bulgularının da olduğu ve ayırıcı tanıda dikkate alınması gerekliliği vurgulanmıştır.

Anahtar Kelimeler: COVID-19; Ürtiker; Anjiyoödem

INTRODUCTION

COVID-19 disease caused by the SARS-CoV-2 virus, which has affected the entire world, can cause clinical manifestations ranging from mild cold symptoms to severe lower respiratory tract infections that can be fatal^[1]. As in recently published cases, some cutaneous findings have been shown to be associated with COVID-19 disease^[2-4]. These findings include urticaria/angioedema, maculopapular rashes, vesicular rashes, sacral ulcers, Chilblain (pernio)-like acral lesions, petechiae/purpura, and livedo reticularis^[3-6]. Here, a COVID-19 case presenting with urticaria and angioedema is described with an informed consent form obtained from the patient.

CASE

On 19.11.2020, a 26-year-old female patient diagnosed with COVID-19 in an external center (tested for being in contact without any complaints, SARS-CoV-2 polymerase chain reaction (PCR) result was detected positive) consulted to our polyclinic with complaints of itchy, erythema

lesions in her body, swelling in the eyes and throat for four days. It was learned from the patient's medical history that the patient did not have any chronic disease or such a complaint before, and the patient received 5-day favipiravir, vitamin C, vitamin D, and treatment with acetylsalicylic acid, and itchy lesions starting on the hands and feet, then spreading to the knees, elbows and the whole body which developed 4 days after the treatment, and swelling in the eyes and throat and difficulty in swallowing were present 1 day after the onset of the rashes. The patient stated that she went to the emergency department with these complaints and received symptomatic treatment, but her complaints did not resolve.

Patient's complaints, according to the history and physical examination, were evaluated as urticaria and angioedema by consulting the dermatology clinic, and food and drug allergies, insect bites, and chemicals were excluded by questioning in the differential diagnosis for etiology. It was learned that she did not use any drugs for 4

days when the complaints began, and she did not consume any different nutrients. Blood tests revealed white blood cell: 15.2×10^3 uL (eosinophils: 0.07×10^3 uL), platelet: 258×10^3 uL, LDH (Lactate Dehydrogenase): 163 U/L, CK (creatin kinase): 55.9 U/L, CRP: 2.1 mg/L, Ferritin: 77 ng/mL, D-dimer: 583 ng/mL, and total IgE: 94.9 IU/mL. All values, except D-dimer and high white blood cell count, were determined to be within normal limits and vital signs were normal. Skin examination showed bilateral swelling of the

eyelids (Figure 1a), erythematous, skin-raised urticaria plaques on the face, legs (Figure 1b), arms, and palms (Figure 1c).

The patient was treated with systemic corticosteroids and antihistamines, and on the 3rd day of treatment, edema in the eyes completely regressed, and urticaria plaques withered. It was recommended to discontinue the corticosteroid therapy on the 3rd day and continue to antihistamine therapy, and all urticaria plaques disappeared on the 7th day of treatment.



Figure 1. Dermatological involvement in the case of COVID-19. A; face, B; legs, C; palms.

DISCUSSION

As experience with COVID-19 has increased, studies have shown that the virus affects other organs, such as the renal, cardiovascular, gastrointestinal, and neurological systems, as well as respiratory diseases^[1,3]. Recently, reports of dermatological findings associated with COVID-19 have been increasing^[2-4]. These findings include lesions such as maculopapular and vesicular rashes, urticaria/angioedema, Chilblain (pernio) - like acral lesions, sacral ulcers, petechiae/purpura, and livedo reticularis^[2-4,6]. Dermatologic findings may occur simultaneously with the classic symptoms of the disease (e.g., fever, cough, sore throat, shortness of breath) or before and after the symptoms^[6-8]. A study conducted with 375 patients in Spain has stated that skin signs associated with COVID-19 may occur at different times of the disease, at different periods of time, and possibly be associated with the severity and prognosis of the disease^[6]. A recent review of skin findings in COVID-19 patients has suggested that cutaneous findings may be useful in triage and risk classification of the patients, while itchy urticaria has diagnostic significance as an early symptom in patients^[9].

Urticaria is one of the most reported skin findings associated with COVID-19^[5-7]. In a study including 88 COVID-19 patients in Italy, it has been reported that 18 (20.4%) patients had skin symptoms and 3 of them had urticaria^[7]. A review by Algaadi, including 30 articles, has identified a total of 202 cases of COVID-19 associated urticaria^[5]. In France, a 27-year-old female patient who consulted with odynophagia, arthralgia, itchy lesions and was diagnosed with urticaria, was found positive in SARS-CoV-2 PCR test which was taken after 48 hours due to fever, chest pain, lymphopenia and CRP height in blood tests^[8].

COVID-19-associated angioedema has been reported rarer than urticaria^[9]. Khalid Hassan has identified a 46-year-old case of urticaria/angioedema, complaining of swelling in his lips, widespread urticaria plaques on his face, torso, and extremities before being diagnosed with COVID-19^[10]. In an article by Shahad et al.,

a patient described as having complaints of mild dry cough and shortness of breath for 5 days was diagnosed with COVID-19 after being admitted to the emergency department due to swelling of the lips, eyes, common itchy lesions that began 1 day ago^[9]. In most cases, urticaria and angioedema were seen to develop before or simultaneously with the classic symptoms of the disease^[5,6,8-10]. However, in one case reported by Adelico et al., the patient had widespread urticaria and angioedema on the 11th day of the disease after being diagnosed with COVID-19, and the symptoms decreased^[11]. Our patient, on the other hand, developed urticaria and angioedema 8 days after diagnosis, without any symptoms. This situation suggests that the disease can also manifest itself with a different finding without common symptoms of disease (cough, sore throat, fever, shortness of breath). All generally reported cases of urticaria/angioedema responded positively to antihistamine therapy with or without systemic/topical steroids^[7-11]. Also, our patient showed a marked decline in complaints on the 3rd day of antihistamine and systemic corticosteroid therapy and complete recovery on the 7th day.

Although the pathogenesis of dermatological findings in COVID-19 has not yet been fully clarified, a study conducted in 2016 suggested that viral infections may be an etiological agent for chronic or acute urticaria^[12]. But in this study, the role of viral infections in the pathogenesis of urticaria was not specified. In a retrospective study by Akarsu et al., it has been shown that, among the factors accompanying chronic urticaria and urticarial vasculitis cases, the most common one is the infectious diseases, of which the most common one is the upper respiratory tract infections^[13]. In a study, it is suggested that SARS-CoV-2, with causing activation of mast cell, leads to the release of chemical components such as histamine, proteases, and interleukins such as IL-1, IL-6, IL-33, whereas in another study it is suggested that ACE2 enzyme is necessary for the inhibition of des-Arg^[9] bradykinin, which is a powerful ligand of bradykinin receptor 1 (B1R), and its inactivation with SARS-CoV-2 causes the activation of bradykinin

and angioedema (14,15). In a study investigating ACE2 expression in different human tissues, it has been shown that ACE2 expression was positive in the lungs, liver, kidneys, brain and on the skin, like many other organs^[16]. In a study investigating microvascular damage and thrombosis in the pathogenesis of COVID-19, 5 patients with purpuric skin rashes have been shown to have an accumulation of C5b-9 and C4d in skin biopsies taken from both lesions and normal-looking skin^[17]. An article that theoretically divides the pathogenesis of the disease into 3 phases (viral, immunogenic, hemovascular) suggests that anaphylatoxins, formed by triggering the classical complement pathway of immune complexes formed in the immunogenic phase, may cause histamine release and mast cell degranulation, and thus a systemic proinflammatory response^[18]. Given all these studies, it can be assumed that some rashes may be directly associated with the viral effect, and some may be associated with the immune response. In our case, urticarial lesions starting from the second week may have occurred due to immune response. However, more studies are needed to prove this idea. Although there is no known drug allergy of the patient, it was considered that the recent history of drug usage due to COVID-19 may also trigger urticaria and angioedema.

CONCLUSION

While the effects of COVID-19 disease still continue all around the world, early recognition of the disease and prevention of its spread are crucial. For this reason, it should be known that it also has atypical symptoms such as urticaria/angioedema. Especially, it should be reminded that new onset urticaria, which cannot be explained with any reason, can sometimes be the earliest or even the only sign of the disease. In addition, further research should also be done on whether there are other symptoms, such as urticaria and other dermatological lesions.

CONFLICT of INTEREST

The authors have disclosed that they do not have any potential conflicts of interest.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: İA, SK

Analysis/Interpretation: SK

Data Acquisition: İA, SK

Writing: İA, SK

Revision and Correction: İA, SK

Final Approval: SK

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