Respir Case Rep 2021;10(2): 87-91 DOI: 10.5505/respircase.2021.98216

A Case of Vasculitis Delayed Due to COVID-19 Differential Diagnosis

Covıd-19 Ayırıcı Tanısı Nedeniyle Geciken Bir Vaskülit Olgusu

Damla Serçe Unat, Aysu Ayrancı, Gülru Polat, Gülistan Karadeniz, Melih Büyükşirin

Abstract

The COVID-19 disease – which emerged in Wuhan, China in December 2019 – has had a significant effect on the whole world having developed into a pandemic, with a wide range of symptoms ranging from asymptomatic carrier to mortality. The focus on COVID-19 diagnosis for these reasons has led to difficulties in the diagnosis and treatment of other diseases. Vasculitis is a very difficult disease group due to its multi-organ involvement and different clinical courses. Due to its radiological properties, there the differential diagnosis of COVID-19 can be difficult. A 65-year-old female patient was admitted with a complaint of dry cough, shortness of breath when walking and chest pain. The patient was examined many times for COVID-19, both in our hospital and in other clinics, and for this reason, the diagnosis of vasculitis was delayed. A diagnosis of vasculitis should be kept in mind in patients with prolonged and multi-systemic symptoms when examined with a pre-diagnosis of COVID-19.

Key words: *COVID-19, vasculitis, granülomatosis with polyangitis.*

Özet

Çin'in Wuhan kentinde 2019 Aralık ayında ortaya çıkan COVID-19 hastalığı, salgın oluşturması ve asemptomatik taşıyıcılıktan mortaliteye kadar oldukça geniş yelpazede semptomlar göstermesi nedeni ile tüm dünyada önemli bir yer edinmiştir. Bu nedenlerden dolayı COVID-19 tanısına yoğunlaşılması, diğer hastalıkların tanı ve tedavisinde bazı zorluklar ve gecikmelere neden olmuştur. Vaskülit, çoklu organ tutulumu ve farklı klinik seyirleri ile tanı ve tedavisi oldukça zor bir hastalık grubunu oluşturmaktadır. Radyolojik özellikleri nedeniyle de COVID-19 ayırıcı tanısında güçlük yaşanmaktadır. Altmış beş yaşında kadın hasta, kuru öksürük, yürümekle olan nefes darlığı ve göğüs ağrısı şikayetleri ile başvurdu. Hasta dış merkezde ve kliniğimizde birçok kez COVID-19 açısından tetkik edildi. Bu nedenle vaskülit tanısında gecikildi. COVID-19 ön tanısı ile tetkik edilen, uzun süreli ve multisistemik semptomları olan hastalarda vaskülit tanısı da akılda tutulmalıdır.

Anahtar Sözcükler: *COVID-19, vaskülit, granülomatoz polianjit.*

Department of Pulmonology, Health Sciences University Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital, İzmir, Turkey

Sağlık Bilimleri Üniversitesi İzmir Dr. Suat Seren Göğüs Hastalıkları Ve Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları Anabilim Dalı, İzmir

Submitted (Başvuru tarihi): 18.11.2020 ***Accepted (Kabul tarihi):*** 15.02.2021

Correspondence (İletişim): Damla Serçe Unat, Department of Pulmonology, Health Sciences University Dr. Suat Seren Chest Diseases and Chest Surgery Training and Research Hospital, İzmir, Turkey

e-mail: sercedamla@gmail.com

Since the first reports of COVID-19 pneumonia in Wuhan, China in December 2019, COVID-19 has spread rapidly around the world. It can progress with mild symptoms such as cough and sore throat, or with pneumonia, respiratory distress, acute respiratory distress syndrome and death. Debates continue on the most appropriate diagnosis and treatment. Diagnoses of COVID-19 are based on the molecular testing of upper and lower respiratory tract tests (1). It is understood that negative virus diagnostic tests do not exclude a diagnosis of COVID-19. The updated IDSA (Infectious Diseases Society of America) guidelines for the diagnosis of COVID-19 describe an algorithmic approach based on patient symptoms, suspicion of infection, lower respiratory tract samples and radiological findings (1-3). Therefore, radiological findings and polymerase chain reactions (PCR) or rapid antibody tests may not always show a correlation in diagnosis. This situation presents us with difficulties in patient management as clinicians. There have been studies stating that Positron Emission Tomography/Computed Tomography (PET-CT) can contribute to the early diagnosis of COVID-19, and can detect it before a nasal carriage. In a case report published by Allen et al. in the United States, it was reported that PCR positivity was detected in the 4th combined nasal and throat swab taken on the 33rd day after a PET-CT image of the patient was taken (4). Thus, COVID-19 findings and differential diagnoses have gained importance in radiological imaging (5). Skin manifestations known to occur in viral diseases, and these symptoms sometimes have diagnostic or prognostic value. Skin lesions such as morbilliform rash, urticaria, vesicular eruptions, acral lesions and livedoid eruptions have been reported in COVID-19 (6).

Vasculitis is a group of diseases that are characterized by inflammation in the vessel wall, and by bleeding, necrosis and granuloma. Radiological findings mainly develop due to ischemia in the area supplied by the vessel. In lung involvement, permanent or temporary nodular or cavitary lesions are seen. The nodular lesions may be mass lesions with sharp margins, or consolidated with uncertain borders. The boundaries, number, shape and clarity of the lesions may vary. Peribronchial thickening, thickening of interlobular septa, and patchy consolidation can be seen in some subtypes of vasculitis (7). Due to these radiological findings, vasculitis should consider in a differential diagnosis of COVID-19.

We report here on a case who was referred to our hospital with a pre-diagnosis of COVID-19 pneumonia, but who was subsequently diagnosed with vasculitis. We present this case to highlight that diagnoses rather than COVID-19 should not be overlooked in the presence of bilateral pulmonary lesions.

CASE

Informed consent was obtained from the patient. A 65-year-old male patient presented with a 1-month history of dry cough, shortness of breath and pain in the legs when walking. A physical examination of the patient revealed diffuse rales in both lungs upon auscultation.

There was no additional disease other than psoriasis in the patient's history. He was not using any additional medication for psoriasis. The patient, who had a smoking history of 45 pack years, had quit smoking 40 days earlier. There were no points of interest in his family history. He had been hospitalized for 5 days with suspicion of COVID-19 in another hospital with the same complaints 2 weeks earlier, and had been discharged after COVID-19 tests were negative. Upon the continuation of complaints, he applied to a different medical clinic and was re-hospitalized with suspected COVID-19 and started on hydroxychloroquine treatment with a diagnosis of possible COVID-19. On the 9th day of hospitalization, the patient left that hospital with after declining treatment and applied to our hospital.

Upon admission, a posteroanterior (PA) chest radiography revealed an increase of heterogeneous opacity localized bilaterally in the lower lung zones (Figure 1). A thoracic high-resolution computed tomography (HRCT) reveled diffuse centriacinar and panlobular emphysema areas in bilateral lung parenchyma and subpleural peripheral located in the bilateral lung parenchyma, mainly in the lower lobes, with surrounding fibroreticular densities and consolidative opacities associated with pleura in the right lower lobe a lesion that could not be distinguished from soft tissue was observed (Figure 2a and b). A PET-CT has been reported to be compatible with benign processes.

The patient's biochemical results revealed mild anemia (hemoglobin 10.3 gr/dL), lymphopenia (400/μL) and urea (140.2 mg/dL), creatinine (2.68), aspartate transaminase (57U/L), alanine aminotransferase (78 U/L) and lactate dehydrogenase (254 U/L) elevation. Also, CRP; 12.88 mg/dL, Ferritin; 2172.7 ng/mL and increased in favor of infection. While d-dimer was immeasurably high, INR was found to be borderline high at 1.22. The patient was hospitalized with a pre-diagnosis of COVID-19, malignancy and vasculitis. A combined nasal and throat swab for COVID-19 PCR was negative. Rapid antibody

IgG and IgM produced a negative result. The patient was started on broad spectrum antibiotherapy. His urine output was followed closely, and intravenous fluid replacement was performed. A complete urinalysis was performed, and two positive (++) proteinuria and erythrocyteuria were observed. The patient underwent internal medicine and nephrology consultations. An abdominal and renal ultrasonography was performed, and Grade 3 hydronephrosis and mild atrophy were observed in the left kidney. Emergency hemodialysis was not considered. In terms of nephrology, outpatient clinic control was recommended under elective conditions.

Figure 1: *Bilaterally heterogeneous opacity*

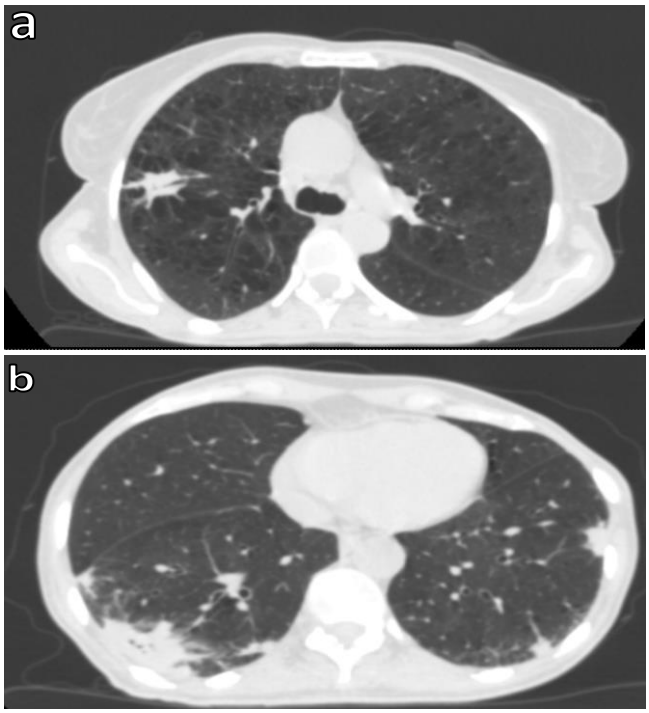

Figure 2a and b: *Bilaterally emphysema and consolidative opacities*

A CT-guided transthoracic fine needle biopsy was performed on the lesion in the lower lobe of the right lung. Biopsy resulted in accordance with the infectious process. The patient, who was thought to have polyserositis and had who had high D-dimer and troponin levels, was consulted with cardiology, but no cardiological problem was considered in the foreground.

Figure 3a and b: *Lessions in joint areas*

In the follow-up of the patient, purpuric and ulcerative lesions were identified in the bilateral lower and upper extremity proximal areas, compatible with the joint areas. Photographs taken with written consent are shown in figures 3a and 3b. Rheumatological markers sent with a pre-diagnosis of vasculitis; PR3 ANCA (Cytoplasmic Antineutrophil Cytoplasmic Antibodies) were three positives (+++) at 1/10 dilution, PM- Scl (+), ANA (Antinuclear Antibody) 1/100 in borderline.

The patient was referred to the internal medicine clinic with a pre-diagnosis of vasculitis. Plasmapheresis and simultaneous dialysis programs were applied four times with a diagnosis of Granulomatosis with polyangiitis in the internal medicine clinic. Cyclophosphamide was given with pulse steroid therapy. Maintenance corticosteroid treatment was arranged, and the patient is still being followed up and treated in an external center.

DISCUSSION

Vasculitis is a disease group with multiple organ involvement, and so patients present with many different symptoms. Vasculitis with pulmonary involvement can be difficult to manage due to the need to exclude such predidiagnoses as pneumonia and malignancy in the pulmonology clinic, and due to the simultaneous multi-organ involvement. The COVID-19 pandemic has made vasculitis difficult to diagnose in patients with bilateral lung lesions on radiological imaging, as other possible diagnoses are ignored. The differential diagnosis of COVID-19 and rheumatological diseases has become very difficult due to similar symptoms, and laboratory and radiological features (8).

Defining the radiology of bilateral lung lesions, especially during the pandemic, and distinguishing the radiological findings of COVID-19 from those of other diseases will guide patient management.

Peripheral and multilobar ground glass opacities are common in COVID-19 patients, and are generally more prominent in the lower-middle lobes and posterior lung areas. While ground glass is more common in the initial stage of the disease, consolidation and crazy paving are more common in the later stages. During recovery from the disease, these ground glass areas may be seen as a fibrotic bands or atelectasis. Due to the increase in thromboembolic events during the course of COVID-19, pulmonary thromboembolism can be seen in thoracic angio CT images in these patients. Pleural effusion, nodule, and inverted halo findings are rarer presentations (9).

Upon observing increased bilateral opacity on chest radiography, a thorax HRCT was performed. Although bilateral lung lesions are not typical for COVID, the patient was evaluated primarily as COVID. Despite the PCR negativity in many different centers, the diagnosis of COVID could not be excluded in the patient. The patient was isolated and was even placed on hydroxychloroquine treatment, due to the suspected COVID. In the last center to which he applied, it was attempted to eliminate COVID initially by isolating. In the patient who also had PCR negativities, COVID could be excluded when the COVID rapid antibody test occurred with Ig M and Ig G negativity. As a result, the actual diagnosis was delayed. Furthermore, the presence of purpuric and ulcerative lesions on the patient's skin made differential diagnosis difficult, as they can be seen in both vasculitis and COVID-19. The skin lesions occurring with COVID-19 can be attributed to various mechanisms, and can include urticarial rashes, confluent erythematous/maculopapular rashes, papulovesicular exanthem, livedo reticularis and purpuric patterns (6).

Considering all these features, the differential diagnosis of the two diseases is very important, and it should not be forgotten that these two diseases can coexist (10). In addition, there are publications in the literature reporting vasculitis and COVID-19 false positivity together (11). All of these indicate that vasculitic diseases and COVID-19 diagnoses should be kept in mind in differential diagnosis or in cases when they are seen together.

CONCLUSION

In these days of the COVID-19 pandemic, the need to exclude a diagnosis of COVID-19 first may lead to delays in actual diagnoses. Vasculitis should be among the preliminary diagnoses considered in cases with suspected COVID-19, when COVID-19 tests are negative, treatment is non-responsive and multiple system symptoms are seen.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - D.S.U., A.A., G.P., G.K., M.B.; Planning and Design - D.S.U., A.A., G.P., G.K., M.B.; Supervision - D.S.U., A.A., G.P., G.K., M.B.; Funding - G.P., M.B.; Materials - G.K., A.A.; Data Collection and/or Processing - D.S.U., A.A.; Analysis and/or Interpretation - D.S.U.,

G.P.; Literature Review - G.K., G.P., D.S.U.; Writing - D.S.U., M.B.; Critical Review - G.K., G.P.

YAZAR KATKILARI

Fikir - D.S.U., A.A., G.P., G.K., M.B.; Tasarım ve Dizayn - D.S.U., A.A., G.P., G.K., M.B.; Denetleme - D.S.U., A.A., G.P., G.K., M.B.; Kaynaklar - G.P., M.B.; Malzemeler - G.K., A.A.; Veri Toplama ve/veya İşleme - D.S.U., A.A.; Analiz ve/veya Yorum - D.S.U., G.P.; Literatür Taraması - G.K., G.P., D.S.U.; Yazıyı Yazan - D.S.U., M.B.; Eleştirel İnceleme - G.K., G.P.

REFERENCES

1. Parikh BA, Bailey TC, Lyons PG, Anderson NW. The brief case: "Not Positive" or "Not Sure"COVID-19-negative results in a symptomatic patient. J Clin Microbiol 2020; 58:1195-20. [CrossRef]
2. Winichakoon P, Chaiwarith R, Liwsrisakun C, Salee P, Goonn A, Limsukon A, et al. Negative nasopharyngeal and oropharyngeal swabs do not rule out COVID-19 Vol. 58, Journal of Clinical Microbiology. Am Soc Microbiology 2020; 58:297-20. [CrossRef]
3. IDSA Home [Internet]. [cited 2020 Sep 13]. Available from: https://www.idsociety.org/.
4. Mo A, Brodin NP, Tomé WA, Garg MK, Kabarriti R. COVID-19 incidentally detected on PET/CT during work-up for locally advanced head and neck cancer. In Vivo 2020; 34:1681-4. [CrossRef]
5. Páez-Granda D, Chicaiza Maldonado M, Calle GS, Ávalos García C, Cabezas Tapia H, Andrade Herrera J. Diagnosis of patients with suspected COVID-19: What is the role of chest CT? Med Clin (Barc) 2020; 155:93. [CrossRef]
6. Young S, Fernandez AP. Skin manifestations of COVID-19. Cleve Clin J Med 2020; 87. [CrossRef]
7. Ödev K. Toraks Radyolojisi | Radyoloji Kitapları. 2nd ed. Vol. 1. Nobel Tıp Kitabevleri; 2010. 201-202.
8. Ciaffi J, Meliconi R, Ruscitti P, Berardicurti O, Giacomelli R, Ursini F. Rheumatic manifestations ofCOVID-19: a systematic review and meta-analysis. BMC Rheumatol 2020; 4:65. [CrossRef]
9. Ufuk F, Savaş R. Chest CT features of the novel coronavirus disease (COVID-19). Turkısh J Med Sci. 2020; 50(4):664-78. [CrossRef]
10. Shenavandeh S, Sefidbakht S, Iranpour P, Teimouri A, Hooshmandi S, Hooshmandi S, et al. COVID-19 and granulomatosis with polyangiitis (GPA): a diagnostic challenge. Rheumatology (Oxford) 2020; 59:2171-3. [CrossRef]
11. Tzouvelekis A, Karampitsakos T, Krompa A, Markozannes E, Bouros D. False positive COVID-19 antibody test in a case of granulomatosis with polyangiitis. Front Med (Lausanne) 2020; 7:399. [CrossRef]