

Ground Glass Opacities Differential Diagnosis in COVID-19 Pandemic: A Case Report

COVID-19 Pandemisinde Buzlu Cam Ayırıcı Tanısı: Bir Olgu Sunumu

 Ceren Degirmenci

Abstract

The pandemic has predisposed all healthcare professionals to assess all viral pneumonia cases preliminarily as COVID-19, with a definitive diagnosis of COVID-19 made on the basis of a positive RT-PCR result. Occasionally, however, there are cases with negative RT-PCR test results both with thoracic CT findings indicative of COVID-19. It is thus very important to consider immunosuppressive conditions and other viral types of pneumonia in the differential diagnosis in patients who do not seem to respond to COVID-19 treatments. We present her a case of HIV infection identified in a differential diagnosis of ground glass opacities.

Key words: COVID-19, pneumonia, HIV, AIDS, CMV, PCP.

Öz

Pandemi, doktorların tüm viral pnömonileri birinci ön tanı olarak COVID-19 olarak değerlendirmeye yatkın hale getirmiştir. COVID-19'un kesin tanısı, pozitif bir RT-PCR testi ile konur, ancak bazen RT-PCR test sonuçları negatif olan, fakat COVID-19'u gösteren toraks BT bulguları olan olgular da vardır. Bu nedenle, COVID-19 tedavilerinden fayda görmeyen hastalarda ayırıcı tanıda immünsupresif sebeplerin ve diğer viral pnömonilerin araştırılması çok önemlidir. Buzlu cam opasiteleri ayırıcı tanısında HIV enfeksiyonu saptanan bir olgu sunulmuştur.

Anahtar Sözcükler: COVID-19, pnömoni, HIV, AIDS, CMV, PCP.

Health Sciences University Atatürk Sanatoryum Research and Training Hospital, Ankara, Türkiye

Sağlık Bakanlığı Üniversitesi Atatürk Sanatoryum Eğitim ve Araştırma Hastanesi, Ankara

Submitted (Başvuru tarihi): 05.04.2022 **Accepted (Kabul tarihi):** 11.06.2022

Correspondence (İletişim): Ceren Degirmenci, Health Sciences University Atatürk Sanatoryum Research and Training Hospital, Ankara, Türkiye

e-mail: cerencekeli@hotmail.com

*This case report was presented as an e-poster at the Turkish Thoracic Society 24th Annual National Congress, which was held between November 17-22, 2021.



Millions of people have been infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since the disease caused by the virus – COVID-19 – emerged in the city of Wuhan in China in December 2019. A definitive diagnosis of COVID-19 is based on the detection of a reverse transcription polymerase chain reaction (RT-PCR) of SARS-CoV-2-specific ribonucleic acid (RNA) in the secretions of the patient suspected of having COVID-19 in samples obtained via such methods as throat-nose swab and tracheal aspirate (1,2). The specificity of RT-PCR for the diagnosis of COVID-19 is high, while its sensitivity is relatively low (3). COVID-19 patients may be asymptomatic or present with non-specific symptoms such as cough, malaise, fever and shortness of breath. Imaging methods are frequently used for the examination of patients with suspected COVID-19 due to the moderate to severe respiratory complaints, as they provide significant benefits in the diagnosis of pneumonia, for evaluations of the degree of spread, the investigation of possible complications such as pulmonary embolism or pneumothorax, the follow-up of patients and the guidance of differential diagnosis. The most common thoracic CT findings in COVID-19 pneumonia are ground-glass opacification and areas of consolidation areas that are indicative of bilateral, peripheral and basal dominant distribution (4). That said, these findings are common to many other infectious or inflammatory diseases, and so it is of great importance to know the differential diagnoses and the clinical and radiological differences between COVID-19 pneumonia and other causes, and to not overlook other viral infections in the differential diagnosis of ground-glass opacity during the pandemic.

CASE

A 41-year-old patient with a previous diagnosis of Crohn's Disease presented to the emergency service with shortness of breath, cough and fever. The patient reported shortness of breath and cough for about a month, despite no history of smoking, and stated that the shortness of breath and cough had exacerbated in the last few days, and that a fever had developed. The patient also complained of hematochezia in the last two months, and a loss of 10 kg in weight in the same timeframe. The patient had been diagnosed with Crohn's disease based on a colonoscopy performed 1 month earlier and had been started on oral budesonide treatment. Upon admission, the patient's body temperature was 38.3°C, pulse 105/min, systolic/diastolic blood pressure 120 and 75

mmHg, respectively, and oxygen saturation (SpO₂) 85%. An examination of his respiratory system indicated bilateral rhonchi. His laboratory results were as follows; white blood cell count (WBC): 6910/mm³, lymphocyte count: 1220/mm³, neutrophil count: 5430/mm³, Hemoglobin (Hb): 11.5g/dL, C-reactive protein (CRP): 126 mg/L, D-dimer: 1.59mg/L, ferritin: > 1675 ng/mL and troponin: 6.6 mg/L. The results of liver and kidney function tests were within normal limits. A postero-anterior (PA) chest X-ray revealed clear bilateral sinuses, and no cardiomegaly or clear ground-glass opacification or areas of consolidation (Figure 1). Thorax computed tomography (CT) revealed diffuse ground-glass infiltrates in both lungs that were determined to be more prominent in the right upper lobe; focal aeration increases and parenchymal density differences in both lungs that were more prominent in the left lower zone; and air cysts and paraseptal emphysema areas in the upper zones that were more prominent on the right side (Figure 2). While the patient's imaging findings were compatible with COVID-19 pneumonia, the result of a PCR test was negative and so a second PCR test was performed that also yielded a negative result. The patient was hospitalized with suspicion of COVID-19 and started on nasal oxygen therapy, favipiravir, low molecular weight heparin, prednisolone and levofloxacin treatments. His hepatitis and HIV markers were sent out on the first day of hospitalization as per routine. The anti-HIV test yielded a positive result on the 4th day of hospitalization. The patient's fever could not be alleviated, and so he was started on trimethoprim-sulfamethoxazole treatment with a suspicion of pneumocystis pneumonia (PCP) by the infectious diseases department. The patient was then referred to a health center with an infectious diseases clinic. The result of the cytomegalovirus immunoglobulin G (CMV IgG) antibodies test was positive and his CMV DNA level was 119432 genomes/ml. The patient has since been undergoing treatment as a newly diagnosed HIV-positive and CMV-positive patient.

DISCUSSION

The pandemic has predisposed all healthcare professionals to assess all viral pneumonia cases preliminarily as COVID-19. All patients, who deemed to be suspicious based on their clinical and radiological findings, and that have an indication for hospitalization during the pandemic are hospitalized with a preliminary diagnosis of COVID-19. The case presented here was pre-diagnosed with COVID-19 based on his high CRP, ferritin and D-dimer levels, as well as bilateral ground-glass opacifica-

tion on CT. A definitive diagnosis of COVID-19 is made on the basis of a positive RT-PCR result, although occasionally cases arise with negative RT-PCR test results yet with thoracic CT findings indicative of COVID-19 (5). It is thus very important to consider immunosuppressive conditions and other viral pneumonias in the differential diagnosis of patients who do not seem to benefit from COVID-19 treatments and who do not respond to attempts to alleviate fever.

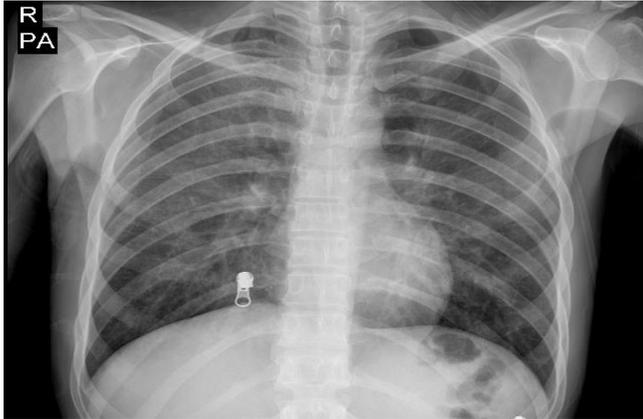


Figure 1: Chest X-Ray

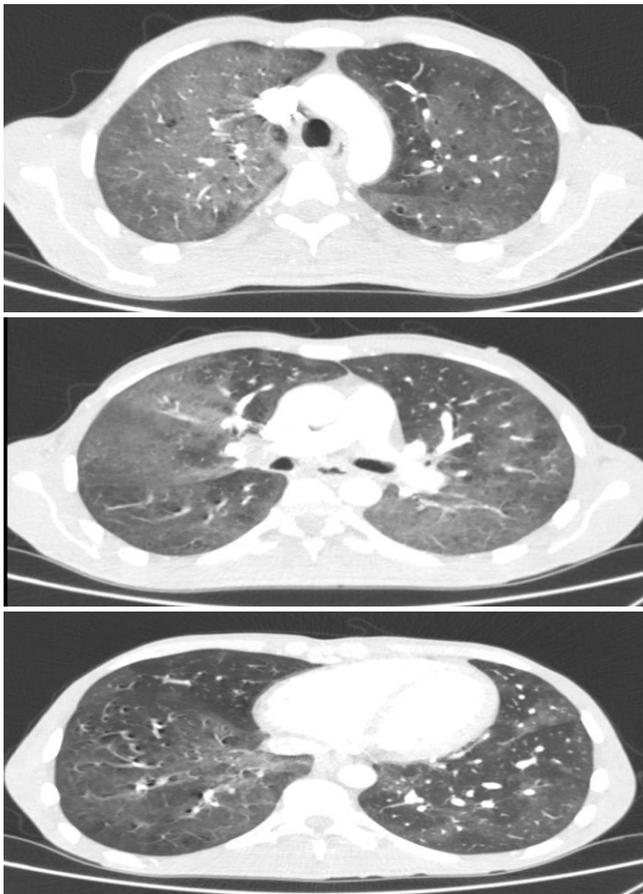


Figure 2: Thorax computed tomography revealing diffuse ground-glass infiltrates in both lungs (determined to be more prominent in the right upper lobe), increased focal aeration and parenchymal density differences in both lungs

There are generally overlaps in the imaging findings of viral pneumonias and those of non-viral infections and inflammatory pathologies, and so it is often difficult to isolate and identify viral pneumonia agents (6-9). A number of imaging findings that may be associated with the pathogenesis of viral infections have been identified, and members of the same virus family have similar pneumonia pathogenesis and radiological findings. CMV pneumonia, as in the case presented here, is frequently seen in immunosuppressed patients and is characterized by irregular ground-glass opacification areas that are scattered or diffusely located in both lungs on thorax CT (6), while COVID-19 pneumonia, in contrast, tends to be more heterogeneous and focal-peripheral (7).

In cases of influenza virus pneumonia, chest radiography and thorax CT findings are generally normal in the vast majority of cases, while the most common findings are more dominant nodules in the mid-upper zones, and areas of focal consolidation and ground-glass opacification around the nodules (6,8). In COVID-19 pneumonia, on the other hand, patchy ground-glass opacification areas with peripheral and multilobar distribution can often be detected in the middle-lower lung zones. Unlike in pneumonia associated with swine flu (hemagglutinin-1 neurominidase-1 [H1N1]), or with the highly pathogenic Asian avian influenza A (H5N1), nodules and consolidation, and areas of ground-glass opacification around the nodules, are not among the findings seen in connection with COVID-19 pneumonia (9). Nasal discharge and flu symptoms are very common in rhinovirus pneumonia, but are seen only rarely in connection with COVID-19 (6). Moreover, fungal infections can also lead to various involvements in the lungs, for example, the PCP caused by the *Pneumocystis jirovecii* fungus is one of the most common opportunistic infections with serious consequences for immunocompromised patients (10). The epidemiology of PCP has increased dramatically with the emergence of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) (11). HIV-associated PCP mostly presents with fever, dry cough, and shortness of breath (12). The clinical symptoms and physical examination findings of PCP and COVID-19 are similar, with diffuse ground-glass opacification areas and accompanying air cysts seen typically in the bilateral upper lobes of the lung in both conditions (7). Both diseases can coexist, and there is potential for a PCP patient to be misdiagnosed with COVID-19, or vice-versa (13). Aside from the infections, cryptogenic organizing pneumonia (COP) and acute interstitial pneumonias should also be

included in the differential diagnosis of ground-glass opacity. Radiological and histopathological findings of COP largely overlap with those of COVID-19. In both cases ground-glass opacification and consolidation areas with peripheral and peribronchovascular distribution are the most common radiological findings, and the reversed halo sign (RHS), also called the atoll sign, are seen in approximately one-fifth of both COP and COVID-19 cases. Furthermore, in both cases lesions in the lung can relocate over time (migratory opacities) (14).

In short, the radiological findings of COVID-19 can be confused with those of many viral pneumonias, and so it would be useful to make a careful differential diagnosis considering the comorbidities and the immune suppressed status of the patient.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - C.D.; Planning and Design - C.D.; Supervision - C.D.; Funding - C.D.; Materials - C.D.; Data Collection and/or Processing - C.D.; Analysis and/or Interpretation - C.D.; Literature Review - C.D.; Writing - C.D.; Critical Review - C.D.

YAZAR KATKILARI

Fikir - C.D.; Tasarım ve Dizayn - C.D.; Denetleme - C.D.; Kaynaklar - C.D.; Malzemeler - C.D.; Veri Toplama ve/veya İşleme - C.D.; Analiz ve/veya Yorum - C.D.; Literatür Taraması - C.D.; Yazıyı Yazan - C.D.; Eleştirel İnceleme - C.D.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China. *N Engl J Med* 2020; 382:727-33. [\[CrossRef\]](#)
2. WHO, CONSTITUTION OF. "World health organization." Responding to Community Spread of COVID-19. Reference WHO/COVID-19/Community_Transmission/2020.1.
3. Kim H, Hong H, Yoon SH. Diagnostic performance of CT and reverse transcriptase polymerase chain reaction for coronavirus disease 2019: a meta-analysis. *Radiology* 2020; 296.3: E145-E155. [\[CrossRef\]](#)
4. WHO. Country & Technical Guidance - coronavirus disease (COVID-19). Geneva: World Health Organization; 2020.
5. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of chest CT and RT-PCR testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology* 2020; 296: E32-E40. [\[CrossRef\]](#)
6. Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. *Radiographics* 2018; 38:719-39. [\[CrossRef\]](#)
7. Ufuk F. COVID-19 pnömonisinde ayırıcı tanı. Savaş R, ed. *Radyoloji ve COVID-19*. 1. Baskı. Ankara: Türkiye Klinikleri; 2020. p.40- 6.
8. Ishiguro T, Takayanagi N, Kanauchi T, Uozumi R, Kawate E, Takaku Y, et al. Clinical and radiographic comparison of influenza virus-associated pneumonia among three viral subtypes. *Intern Med* 2016; 55:731-37. [\[CrossRef\]](#)
9. Ufuk F, Savaş R. Chest CT features of the novel coronavirus disease (COVID-19). *Turk J Med Sci* 2020; 50: 664-678. [\[CrossRef\]](#)
10. Medrano FJ, Montes-Cano M, Conde M, de la Horra C, Respalda N, Gasch A, et al. Pneumocystis jirovecii in general population. *Emerg Infect Dis* 2005; 11:245-50. [\[CrossRef\]](#)
11. Huang L, Morris A, Limper AH, Beck JM. An official ATS workshop summary: recent advances and future directions in Pneumocystis pneumonia (PCP). *Proc Am Thorac Soc* 2006; 3:655-64. [\[CrossRef\]](#)
12. Fujii T, Nakamura T, Iwamoto A. Pneumocystis pneumonia in patients with HIV infection: clinical manifestations, laboratory findings, and radiological features. *J Infect Chemother* 2007; 13:1-7. [\[CrossRef\]](#)
13. Blanco JL, Ambrosioni J, Garcia F, Martínez E, Soriano A, Mallolas J, et al. COVID-19 in patients with HIV: clinical case series. *The Lancet HIV* 2020; 7:e314-6. [\[CrossRef\]](#)
14. Zhao F, Yan SX, Wang GF, Wang J, Lu PX, Chen B, et al. CT features of focal organizing pneumonia: an analysis of consecutive histopathologically confirmed 45 cases. *Eur J Radiol* 2014; 83:73-8. [\[CrossRef\]](#)