

Lung cancer and Lambert-Eaton syndrome concealed by COVID-19

Severe diseases hidden by COVID-19

Selçuk Akan¹, Baran Balca²¹Department of Internal Medicine, Ankara City Hospital, Ankara²Department of Chest Disease, Marmara University Faculty of Medicine, Istanbul, Turkey**Abstract**

COVID-19, which infects millions of people worldwide, can affect many organs and systems, mainly the lungs, heart, brain, kidneys, vascular endothelium and bone marrow. As a result, it causes a wide range of complications such as ARDS, acute coronary syndrome, delirium, pancytopenia, DIC, kidney damage. Therefore, in the presence of COVID-19, some diseases that progress rapidly and which can cause similar complications may be concealed. In our article, we aimed to describe a patient who was missed due to the adverse effects of the pandemic period and because the COVID-19 infection may cause similar findings, although he admitted to emergency clinic twice before. In a pancytopenic patient suffering from intermittent fever, exhaustion, myalgia and arthralgia for several months, the diagnosis of small cell lung cancer, bone marrow metastasis and Lambert Eaton Myasthenic Syndrome (LEMS) was delayed due to the presence of COVID-19 infection. Therefore, the patient died in a short time. It was presented because it is a rare case and can lead to serious consequences if not imagined.

Keywords

COVID-19; Lung cancer; Lambert-Eaton Myasthenic syndrome

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Introduction

The coronavirus pandemic negatively impacted healthcare access and healthcare provision. Most of the hospitals were used for patients affected by the pandemic, and medical teams were assigned to follow up and treat these patients. The number of active outpatient clinics and patients was reduced in all branches. However, avoiding medical assistance due to curfews and fear of COVID-19 also prevented early diagnosis of serious diseases such as cancer.

Cancer patients are relatively elderly, in poor physical condition, often with more than one underlying disease and poor lung function. In patients with lung cancer, there are tumor symptoms, including cough, sputum, dyspnea and even fever, and all of these symptoms can be also seen in lung infections. Therefore, COVID-19, which can cause rapid and widespread lung involvement in lung cancer cases that have not yet been diagnosed, may mask cancer clinically and radiologically and may delay diagnosis. On the other hand, symptoms of COVID-19 infection in patients with cancer are more severe and can quickly worsen the clinic [1].

Lung cancers are the most common tumors associated with paraneoplastic syndromes. Lambert-Eaton Myasthenic Syndrome (LEMS) is the most common neurological paraneoplastic syndrome. Small cell lung cancer was detected in 60% of all patients presenting with LEMS [2].

Small cell lung cancer has the feature of doubling time, high growth fraction and early metastasis, hematogenous metastasis is present in 2/3 of the cases during diagnosis [3].

As a matter of fact, the patient, who was admitted to the emergency department with various complaints for a few months and was treated on an outpatient basis due to COVID-19 infection, was hospitalized to our internal medicine clinic due to COVID-19 pneumonia and pancytopenia as his complaints worsen. In addition to COVID infection, small cell lung carcinoma bone marrow metastasis and LEMS were detected in further examinations. It was presented to raise awareness, as it is a rare situation in the adverse conditions of the pandemic period and has fatal consequences when overlooked.

Case Report

A 53-year-old male patient without known systemic disease, admitted to the emergency service 2 months ago with weakness, back pain and mild weakness in the legs. In his examinations, Hb: 11.3 g/dl, Plt: 135000 /mm³, CRP: 15 mg /L. Oral iron preparation and non-steroidal anti-inflammatory drug were prescribed to the patient. The patient whose complaints continued to increase despite the medications, had an intermittent fever and admitted to the emergency department 15 days ago with these complaints. Here, favipiravir and paracetamol were administered to the patient, whose COVID test was positive and mild involvement in the lower lobes was detected on chest X-ray, as O₂ saturation was normal. Despite the medication, the patient's complaints continued and dyspnea started. The patient referred to our internal medicine outpatient clinic with complaints of increasing back and lumbar pain, progressive muscle weakness and fever for 2 months. The patient had a smoking history of 40 packs/year. There was no feature in his family history.

WBC: 3.400 /mL, Hb: 9.8 g/dl, Plt: 81.000 /mm³, sedimentation: 80 mm/hour, CRP: 60 mg/L, Na: 132 mEq/L, K: 3.6 mEq/L, ALP: 112 U/L, AST: 97 U/L, ALT: 62 U/L, LDH: 885 U/L, GGT: 121 U/L, D-dimer 0.40 µg/mL, COVID-19 PCR (+) was detected in blood analysis. The chest X-ray showed low-density pneumonia foci, which mostly involved bilateral middle and lower zones (Figure 1). The patient was admitted to the internal medicine clinic for the investigation of COVID-19 pneumonia and pancytopenia. Positive pressure oxygen, erythrocyte suspension replacement, methylprednisolone, enoxaparin sodium, Plaquenil (previously taken favipiravir) treatment was initiated in the patient whose saturation was measured as 85% in room air. In the peripheral blood smear examination, 55% PNL, 25% lymphocyte, 4% monocyte, 2% eosinophil, 9% normoblast, 1% myelocyte, 2% metamyelocyte, 2% myeloblast were seen. A bone marrow biopsy was performed on the patient, who was consulted to the hematology clinic.

In the follow-up, the patient's muscle enzymes CK: 1166 mcg/L, CKMB: 92 mcg/L were found to be higher, with progressive loss of strength in the left arm and both legs. Electroneuromyography (ENMG) was performed to the patient, who was consulted to the neurology clinic. In ENMG, a decrease in muscle activity was

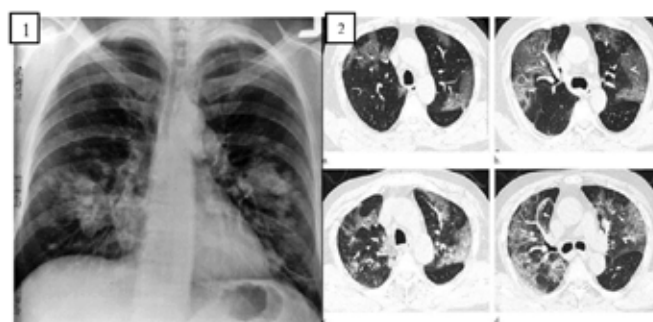


Figure 1. (1) A mass of 25x23 mm with soft tissue density in the left middle lobe and low-density pneumonia foci localized bilateral middle and lower zones of the lung (2) The ground glass opacifications in the form of a multi-patch pattern (a and b); more progressive ground glass areas and air bronchograms after 1 week (c and d)

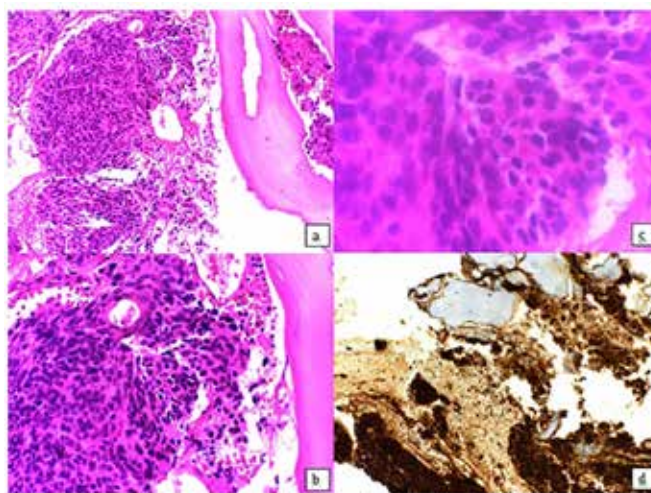


Figure 2. Small cell bronchogenic carcinoma metastasis to the bone marrow tissue (H&E × 200), small round-tumor cells resembling blastic ones around the lamellar bone (a, b, and c), and positive chromogranin-A immunoreactivity in the tumor cells (d)

detected as a result of repetitive nerve impulses to the biceps brachia, quadriceps and tibialis anterior muscles. Combined Muscle Action Potential amplitudes (CMAP) were detected at normal and lower limits in the nerve conduction study. In the needle EMG, more prominent myogenic motor unit potentials (MUP) were observed in the proximal muscles. In the Repetitive Stimulation (RS) test performed with 3 and 5 Hz, 34% decrement response was observed, and 178 % increment response was observed in RS performed with 50 Hz. It was stated that EMG findings were compatible with LEMS and malignancy screening was recommended.

In bone marrow biopsy, tumoral cells with round oval nuclei infiltrating the marrow, narrow cytoplasm and vesicular nucleus were observed and interpreted as bone marrow metastasis of small cell lung cancer (Figure 2). In the thorax tomography, a mass with a soft tissue density of 25x23 mm in the left middle lobe of the lung and multiple patch-like ground glass-like densities in both lungs were observed. The progression in the lung findings was observed on the patient's subsequent tomography one week later. (Figure 1). Considering the patient's biopsy result and EMG findings, diagnoses of small cell lung cancer, bone marrow metastasis, LEMS and COVID-19 pneumonia were made. In the patient who was given antiviral therapy, oxygen support and erythrocyte suspension, dyspnea increased and O₂ saturations decreased within 1 week. The intubated patient was transferred to the intensive care unit and died 2 days later.

Discussion

Severe acute respiratory syndrome coronavirus (SARS-CoV)-2, a novel RNA coronavirus in the same family as SARS-CoV, was identified in December 2019 as the cause of a pneumonia outbreak affecting Wuhan, China [4]. It worldwide infected 98 million people and killed more than 2.122.000 people up to February 2021 (available at: <https://www.worldometers.info/coronavirus/>). COVID-19 mostly affects the lungs, heart, brain, kidneys, vascular endothelium, and bone marrow and can causes complications in patients such as ARDS, acute coronary syndrome, delirium, pancytopenia, DIC, and kidney injury [4].

The COVID-19 may present with symptoms ranging from asymptomatic to severe respiratory failure and may differ from person to person [5]. Fever, dyspnea, cough, sputum, sore throat, headache, diarrhea, nausea-vomiting, muscle-joint pain and weakness are the most common symptoms in patients [6]. Our patient had similar symptoms.

Smoking, hypertension, chronic kidney disease, cardiac disorder, age older than 65 years and cancer have been identified as risk factors for hospitalization and severe respiratory disease in COVID-19 [7]. Our patient had been smoking 1 pack/day for 40 years and had undiagnosed lung cancer.

Typical thorax CT findings in individuals with COVID-19 were ground-glass opacities, particularly on the peripheral and lower lobes, nontypical CT findings included pleural effusion (only about 5%), masses, cavitations and lymphadenopathies [6,8]. Similar radiological findings were present in our patient. Since the radiological findings were compatible with COVID-19 and there was no dyspnea and the O₂ saturation was normal, the patient did not have thorax tomography at the emergency

admission. Lung cancer was not considered in the preliminary diagnosis, as chest radiography findings can also be seen in COVID-19.

Lung cancer had metastasized to the bone marrow in the 2-months period from the onset of the complaints, and LEMS developed as a paraneoplastic syndrome in the patient with the effect of released mediators and/or autoimmune mechanisms [9]. Since all clinical and laboratory findings, including pancytopenia, can be seen in COVID-19, only antiviral treatment was given to the patient. The patient, whose complaints increased despite antiviral therapy and his laboratory findings worsened, was hospitalized at internal medicine admission.

LEMS is a rare neuromuscular junction disease characterized by proximal muscle weakness, decrease or loss of reflexes, moderate ocular and autonomic findings with antibody development to presynaptic voltage-dependent calcium channels. It can be paraneoplastic or autoimmune [10]. LEMS is a rare neuromuscular conduction disorder and malignancy can be detected in 50-60% of the cases. In our case, it was associated with small cell lung cancer. Neuromuscular symptoms may occur for a few weeks or months before lung cancer is diagnosed.

Clinically; pelvic and thigh muscles fatigue, dry mouth, dysarthria, dysphagia and muscle pain can be seen. In physical examination; ptosis, ocular muscle weakness, reduction and/or loss of deep tendon reflexes can be detected [11]. In our case, before the diagnosis of malignancy, there was a loss of strength in arms and legs.

COVID-19 delayed the diagnosis of cancer and led to rapid deterioration in the clinical condition in the patient with lung cancer, bone marrow metastasis and LEMS. As a result, in some diseases, clinical and laboratory findings may mask more serious diseases similar to them and delay their diagnosis. Therefore, it should be kept in mind that a more serious underlying pathology may be present in patients whose complaints continue for a long time and/or do not respond to treatment. In addition, it should be kept in mind that malignancy may accompany the disease in LEMS cases, and symptoms may be observed even if the tumor is very small.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Yan X, Hongsheng L, Ke H, Mengzhao W. *Clinical Management of Lung Cancer Patients during the Outbreak of 2019 Novel Coronavirus Disease (COVID-19)*. *CJLC*. 2020; 23(3):136-41. DOI: 10.3779/j.issn.1009-3419.2020.03.02.
2. Block JB. *Paraneoplastic syndromes*. In: Haksel CM, editors. *Cancer Treatment*. 4th ed. Philadelphia: WB Saunders; 1995. p. 245-6.
3. Yilmaz Ü. *Treatment Approaches in Lung Cancer*. *Nucl Med Semin*. 2018; 4: 32-8. DOI: 10.4274/nts.2018.005.
4. Jain U. *Effect of COVID-19 on the organs*. *Cureus*. 2020; 12(8): e9540.

DOI:10.7759/cureus.9540.

5. He F, Deng Y, Li W. Coronavirus disease 2019 (COVID-19): What we know? *J Med Virol*. 2020; 92(7):719-25. DOI: 10.1002/jmv.25766.
6. Giuseppe P, Alessandro S, Chiara P, Federica B, Romualdo DB, Fabio C, et al. COVID-19 diagnosis and management: a comprehensive review. *J Intern Med*. 2020; 288(2):192-206. DOI: 10.1111/joim.13091.
7. Robilotti EV, Babady NE, Mead PA, Rolling T, Perez-Johnston R, Bernardes M, et al. Determinants of COVID-19 disease severity in patients with cancer. *Nat Med*. 2020; 26(8):1218-23. DOI: 10.1038/s41591-020-0979-0.
8. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang ZQ, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. *Infect Dis Poverty*. 2020; 9(1):29. DOI: 10.1186/s40249-020-00646-x.
9. Hersby DS, Do TH, Gang AO, Nielsen TH. COVID-19-associated pancytopenia can be self-limiting and does not necessarily warrant bone marrow biopsy for the purposes of SARS-CoV-2 diagnostics. *Ann Oncol*. 2021; 32(1):121-3. DOI: 10.1016/j.annonc.2020.09.020.
10. Say B, Ergün U, Karaca G. Case with atrophy and proximal muscle weakness: seronegative Lambert Eaton Myasthenic Syndrome. *Pam Med J*. 2019; 12:181-3. Doi: 10.31362/patd.453646.
11. Gül Ş, Çetinkaya E, Özgül G, Gençoğlu A, Çam E. Small Cell Lung Cancer With Lambert-Eaton Myasthenic Syndrome: A Case Report. *Göğüs Hastanesi Dergisi*. 2010; 24(1):45-8.

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