



Lung cancer and Lambert Eaton syndrome concealed by COVID-19

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Abstract

COVID-19, which infects millions of people worldwide, can affect many organs and systems, mainly 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're going to tell 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.

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 the 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 as an outpatient due to COVID-19 infection, was hospitalized in our internal medicine clinic due to COVID-19 pneumonia and pancytopenia, as his complaints get worse. 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 have fatal consequences when overlooked.

Case

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

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the medications, had intermittent fever and admitted to the emergency department 15 days ago with these complaints. Here, favipravir 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 /mcL, 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. 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 favipravir) 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 to 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 in the patient 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 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 25 x 23 mm in the left middle lobe of the lung and multiple patch-like ground glass-like densities in both lungs were observed. There was progression in the lung findings in 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. 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 intensive care unit and died 2 days later.

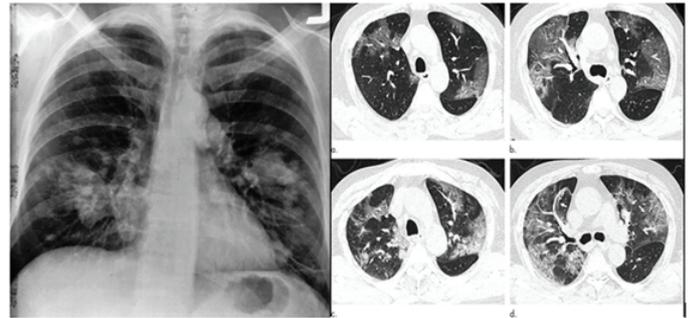


Figure 1. (1) A mass of 25x23 mm having a soft tissue density in the left middle lobe and low-density pneumonia foci localized bilateral middle and lower zones of lung. (2) The ground glass opacifications in the form of multi-patch pattern (a and b); more progressive ground glass areas and air bronchograms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

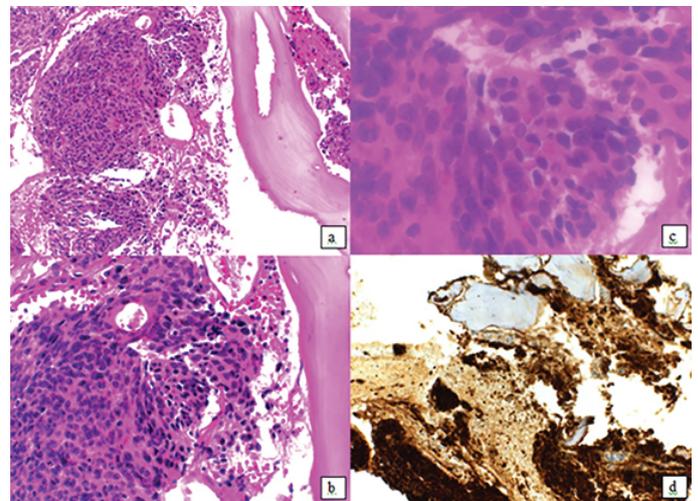


Figure 2. Small cell bronchogenic carcinoma metastasis to the bone marrow tissue (H&E × 200), small round-tumor cells resembling blastic ones around the lamellar bone (a, b, and c), and positive chromogranin-A immunoreactivity in the tumor cells (d).

Results

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. (<https://www.worldometers.info/coronavirus/>). COVID-19 mostly affects the lungs, heart, brain, kidneys, vascular endothelium, and bone marrow and can cause 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 he 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, there was loss of strength in arms and legs before the diagnosis of malignancy.

COVID-19 delayed the diagnosis of cancer and caused the clinical condition to deteriorate rapidly in the patient with lung cancer, bone marrow metastasis and LEMS. As a result, 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.

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