Clinical findings in patients with leprosy who are infected with COVID-19: a case series from Elazığ, Turkey

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Summary

Background: Leprosy is a chronic granulomatous infectious disease caused by *Mycobacterium leprae* that can be self-limiting or progressive according to the immunological status of the host organism.

Aim and objectives: We present the demographic and clinical characteristics of lepromatous leprosy (LL) patients who had Covid-19 infection.

Materials and methods: This study recruited patients hospitalized in Elazığ Leprosy Hospital. Details of the patients were collected as follows: age, gender, presence of comorbidity, leprosy classification, clinical presentation, presence of leprosy reactions and complaints at the time of admission; laboratory and computed tomography (CT) findings and treatments applied.

Results: This study included 9 patients with lepromatous leprosy (LL classification). Six patients were PCR positive for SARS-CoV-2, 7 patients had thoracic CT involvement. The mean age was 78.7 years (range 65–95). Complaints on admission included fatigue (n:7), cough (n:4) and fever (n:3) followed by sore throat (n:1), headache (n:1) and dysphonia (n:1). Two patients were asymptomatic, PCR positivity was detected in one and CT positivity was detected in another during screening. All patients received treatment with favipiravir and enoxaparin. No leprosy reactions occurred. All patients were discharged with recovery after completion of treatment.

Conclusion: We expected that the risk for catching COVID-19 may be higher in LL patients who have a cellular immunity deficiency, and that the course of the infection may be more severe in COVID-19-infected LL patients, for the same reason. However, we have seen a decrease in the clinical severity of the COVID-19 and no patient losses. We conclude that this situation may be due to the drugs used for leprosy treatment.

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These immune-modulating drugs may cause a decrease in the clinical severity of the COVID-19, but we need larger studies on this subject.

Keywords: COVID-19, leprosy, cytokines, comorbidity, hypocalcemia

Introduction

Leprosy is a mycobacterial infection affecting peripheral nerves and the immune system. Although the prevalence and incidence rates for leprosy have been significantly reduced as a result of the control strategies of the World Health Organization (WHO), new cases still appear in the world. It is a serious, chronic, infectious disease that can vastly change a person's life.¹ One of the important points in the course of the COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is how is this virus affects patients with other infectious diseases.¹ The World Health Organization (WHO) reported that there are >130 million confirmed cases of COVID-19 worldwide, resulting in 2,930,732 deaths (2.1%). The reported mortality rate for COVID-19 in Turkey was 1% in the general population.² This article describes the clinical characteristics and outcomes in patients with COVID-19 and leprosy.

Material and methods

This study included LL patients who were infected with Covid-19. Details of the patients were collected as follows: age, gender, presence of comorbidity, leprosy classification, clinical presentation, presence of leprosy reactions and complaints at the time of admission; laboratory and computed tomography (CT) findings and treatments applied.

Results

Nine patients were included in the study, all with the lepromatous clinical form of leprosy. All of them had disability. They are not receiving treatment for leprosy now, but currently only receive treatment for comorbidities such as antihypertensive and antidiabetic treatment. The last leprosy reactions were seen many years ago (approximately 20 years). All of them had confirmed diagnosis of COVID-19 infection. Seven patients had thoracic involvement on CT scan. Ground-glass appearance was present in almost all patients with lung involvement. Six patients were PCR positive for SARS-CoV-2. PCR test results of the remaining 3 patients were negative, but they had a contact history, fever and subpleural multi-focal ground-glass appearance consistent with COVID pneumonia on the CT of the thorax (Figure 1). Therefore, these three patients were evaluated as COVID-19, and their follow-up and treatment was planned. Two of the patients were female and 7 were male. The average age was 78.7 years (range 65–95). Complaints on admission were general weakness, fever and cough. Serum D-dimer levels of 8 patients, serum CRP levels of 7 patients, serum IL-6 levels of 5 patients, serum ferritin levels of 3 patients and serum procalcitonin levels in all 9 patients, were found to be increased. Serum calcium (Ca) levels were low in all patients.

All patients were treated in accordance with the recommendations of the Turkish Ministry of Health COVID-19 (SARS-CoV-2 Infection) Adult Patient Treatment Guidelines.³ All patients were given 1600 mg bid loading dose and 600 mg bid maintenance treatment of favipiravir as antiviral therapy for a total of five days, and enoxaparin was initiated according to the guidelines to prevent blood clots. None of the patients had active bleeding or thrombocytopenia. The treatments that the patients received due to their chronic diseases were continued. Liver

Figure 1. Patchy ground-glass appearances and areas of consolidation in both lower lobes of the lungs.

function tests (AST and ALT) elevation were observed in the follow-up of one patient, and internal medicine consultation was performed. While the oxygen saturation of all patients was 90% and above, only one patient had an oxygen saturation of 86% at room air. Intermittent oxygen was given to this patient through a nasal cannula. The patients were discharged on the 10 day of their hospitalization, after their treatment was completed, their general condition was good and their vital signs were stable. Table 1 shows their clinical and demographic characteristics.

Case 1

An 87-year-old male patient was admitted to the emergency room with fever, cough and shortness of breath. The patient was PCR positive and had lung involvement on thorax CT. The patient had comorbid conditions including diabetes mellitus (DM) and hypertension (HT). Laboratory evaluation revealed elevated D-dimer, CRP, procalcitonin, IL-6 levels and low serum Ca levels. The patient recovered and was discharged after his treatment had been completed.

Case 2

In a 76-year-old male patient who presented with fever and cough, the PCR test was negative, but contact history, clinical and radiological findings suggested COVID-19. Pulmonary involvement was detected. He also had chronic obstructive pulmonary disease (COPD), HT, heart failure, and he was a Hepatitis C virus (HCV) carrier. In the laboratory evaluation of the patient; D-Dimer, C-reactive protein (CRP), procalcitonin, IL-6, ferritin levels were elevated and serum Ca levels were low. Oxygen saturation was 86%, and he was given intermittent oxygen through a nasal cannula.

Table 1. The clinical characteristics of the patients with COVID-19 associated LL

	Sex	Age	Fever	Cough	PCR	CT of the thorax	Comorbidity	D-dimer (0–500 µg/l)	CRP (0–8 mg/l)	Ferritin (24–336 µg/L)	IL-6 (5.3–7.5 pg/mL)	Ca (8.8–10.6 mg/dl)	Procalcitonin (0–0.1 ng/ml)
1	M	87	+	+	+	+	DM, HT	852	63.5	136	26.20	8	0.083
2	M	76	+	+	–	+	COPD, HT, HF, HCV	1880	36.2	802	4.25	8.7	0.110
3	M	77	+	–	+	–	HT, HBV	2220	96.2	230	15.3	8.1	0.024
4	F	77	–	–	+	+	HT, HCV	760	8.96	94	3.61	8.2	0.023
5	F	60	–	+	+	+	–	1010	5.81	174	10.93	8.4	0.048
6	M	82	–	–	+	+	HT	600	178	345	6.1	8.3	0.353
7	M	95	–	–	–	+	–	1390	126	356	9.8	8.2	0.170
8	M	90	–	–	+	–	HT, HCV	346	2	25	2.59	8.6	0.037
9	M	65	–	+	–	+	–	681	24.99	154	15.94	8.7	0.059

Polymerase chain reaction (PCR); Computed Tomography (CT); Heart failure, (HF), Chronic obstructive pulmonary disease (COPD) diabetes mellitus (DM) and hypertension (HT) Hepatitis C virus (HCV), Hepatitis B virus (HBV).

Case 3

A 77-year-old male patient had PCR positivity but no lung involvement. The patient who presented with complaints of fever and weakness had HT and he was a Hepatitis B virus (HBV) carrier. D-dimer, CRP, procalcitonin, IL-6 levels were elevated and serum Ca levels were low.

Case 4

A 77-year-old female patient was admitted with sore throat. The patient, who had PCR positivity, had lung involvement. The patient had HT and HCV carriage. The patient, who was found to have elevated D-dimer, CRP, procalcitonin, and low serum Ca level, was hospitalized and followed up.

Case 5

A 60-year-old female patient was admitted with cough. The patient, who had PCR positivity, had lung involvement. Increase in serum AST, ALT, D-dimer, procalcitonin, IL-6 levels, and low serum Ca level were detected in the patient who had no comorbid conditions.

Case 6

An 82-year-old male patient presented with headache and hoarseness. The patient who had PCR positivity had lung involvement. The patient who had HT had elevated D-dimer, procalcitonin, CRP, low serum Ca levels and normal IL-6 levels.

Case 7

A 95-year-old male patient had negative PCR and pulmonary involvement. The patient, who had no comorbid conditions, had elevated D-dimer, CRP, ferritin, procalcitonin and low serum Ca levels.

Case 8

A 90-year-old male patient had PCR positivity with no pulmonary involvement. HT and HCV were present, serum Ca level and IL-6 level were low, only procalcitonin levels were high. The patient, who had no clinical symptoms, was hospitalized for follow-up purposes.

Case 9

A 65-year-old patient presented with the complaints of cough and weakness. PCR was negative, but contact history, clinical and radiological findings were evaluated in favor of COVID-19. There was lung involvement. Serum D-dimer, elevated CRP, low Ca and IL-6 levels were detected.

Discussion

People of all ages can be infected by COVID-19. However, the elderly and people with preexisting medical conditions appear to be more vulnerable to becoming severely ill with the virus, according to WHO.⁴

It is suggested that the severity of the disease in those who have COVID-19 infection is related to the cytokine storm that develops due to an altered immune response. It has been suggested that increasing IL-6 levels, lymphopenia and decreased CD4 and CD8 rates, are associated with severe lung damage.⁵

Lepromatous leprosy is a clinical subtype that develops as a result of excessive growth of bacilli in people with low cellular immunity. Raised cytokine levels, such as interleukin (IL)-6, IL-10, interferon (IFN- γ), and tumor necrosis factor (TNF)- α , are associated with LL leprosy. In this form, T helper (Th) 2 dominates and the production of IL-4, IL-10 and TGF increases

and the microbicidal response of macrophages is inactivated. In addition, TNF- α and IL-6 production is induced and contributes to the progression of the disease.⁶

Another important focus is the possible increase in the frequency and intensity of the reactional state, as would be expected in cases in which leprosy patients contract other viral infections.⁷ Leprosy reactions are characterized by malaise and the exacerbation of preexisting lesions, with subsequent erythema and pain that are usually accompanied by neuritis and severe edema of the extremities.⁸ Long term corticosteroid use required for treatment of these reactions is a condition that increases the risk for COVID-19.⁴

The inflammatory response plays a critical role in COVID-19, and an inflammatory cytokine storm increases the severity of COVID-19.⁹ IL-6 may have a significant role in classifying various forms of leprosy and can be used as a leprosy disease marker to predict the course and the prognosis of the disease.¹⁰ Cytokines play a role in the etiopathogenesis of both diseases, increasing the importance of this comorbidity.

COVID-19 infection leads to a serious syndrome requiring further hospitalization and assisted ventilation with high lethality although it has a good prognosis in most patients.¹¹ Previous studies have reported that calcium plays a central role in viral infectious and in the replicative mechanisms of SARS-CoV, MERS-CoV, and Ebolavirus.¹¹ Some authors considered hypocalcemia to be an independent risk factor in terms of increased hospitalization and intensive care unit (ICU) admission, severity of disease and death.¹¹ However, contrary to this study, although low serum Ca levels were observed in all of our patients, no severe clinical course was observed. Therefore, it is currently unclear whether the hypocalcemia in COVID-19 is merely a marker of disease severity rather than a specific feature of the disease. The clinical and prognostic significance of this biochemical finding for COVID-19 is still unclear.

The production and release into the circulation of procalcitonin from extrathyroidal sources is enormously amplified during bacterial infections, and is actively sustained by enhanced concentrations of IL-1 β , TNF- α and IL-6. Nevertheless, the synthesis of this biomarker is inhibited by INF- γ , whose concentration also increases during viral infections.¹² Procalcitonin is a useful indicator for bacterial infections, though not all patients with COVID-19 have bacterial co-infections.¹³ Our patients also had co-infection and elevated serum procalcitonin levels.

In another paper about COVID-19 and LL co-infectivity, 4 out of 378 LL patients developed COVID-19 infection and were hospitalized. Their ages ranged between 39–87 years and the F/M ratio was 1/1. Three patients had HT and DM. Their duration of hospital stay was between 1 and 27 days, and all 4 patients died.⁶

In our study, the average age of our patients was higher, they had comorbidities, they had low calcium levels, elevated procalcitonin and IL-6 values, which are accepted as poor prognosis criteria, but they all recovered and were discharged.

Because of the small numbers of cases presented in these studies, it is not possible to reach a conclusion as to whether people affected by leprosy, especially those with lepromatous disease, have an increased susceptibility to COVID-19 and to more severe disease. Further studies with a larger sample size are needed.

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