



COVID-19 in a Patient with Newly Diagnosed Chronic Lymphocytic Leukemia (CLL): A Case Report

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Abstract

Chronic lymphocytic leukemia (CLL) is one of the most common hematologic neoplasms leading to immunosuppression. It is characterized by absolute lymphocytosis with clonality of mature B cells. Therefore, they are vulnerable to various infections especially COVID-19. Little is known about the COVID-19 infection when it unmasks CLL.

We reported a 90-year-old man who presented with signs and symptoms of anorexia, weakness, and loss of consciousness, and lymphocytosis which in further workup COVID-19 confirmed with real-time PCR. Due to lymphocytosis, peripheral blood smear (PBS) and flow cytometry were performed and CLL was diagnosed. His lymphocyte count increased to 1.5-fold during hospitalization. The patient recovered after 11 days as the symptoms were alleviated.

Lymphocytosis is an unexpected finding in patients diagnosed with COVID-19 infection, and an increase in lymphocytes may indicate other conditions. In these cases, secondary causes of lymphocytosis, such as malignancy or other infections, should be considered

Keywords: Coronavirus, COVID-19, Leukemia, Lymphocytic, Chronic

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Introduction

COVID-19 viral infection was first reported in Wuhan, Hubei, China in 2019 and now became one of the most prevalent pandemics in the world. It is also called SARS-CoV-2 since it has the severe signs and symptoms of acute respiratory distress syndrome (ARDS) (1).

Patients with hematological malignancy are susceptible for severe Covid-19. It is found that COVID-19 is more prevalent in patients with hematological cancer compared to solid tumors (2).

Chronic Lymphocytic Leukemia (CLL) is a hematological malignancy that involves mature B lymphocytes. It is the most prevalent leukemia in adults. Patients often have the signs and symptoms of

splenomegaly, lymphadenopathy, cytopenia and lymphocytosis (3).

There are few reports about COVID-19 concomitant with CLL patients. In this case-report, we represented a newly diagnosed case of CLL during COVID-19 infection.

Case presentation:

A 90-year-old man was admitted to the intensive

care unit (ICU), with a 4-day history of anorexia, weakness and loss of consciousness. His past medical history was cerebrovascular accident (CVA) and type 2 diabetes mellitus (DM- II).

Chest CT scan showed peripheral bilateral ground-glass opacities (GGO) with peripheral consolidation. Also, it revealed mediastinal lymphadenopathies in the aortopulmonary window. The real-time PCR test was conducted and was positive for COVID-19 (Figure 1).

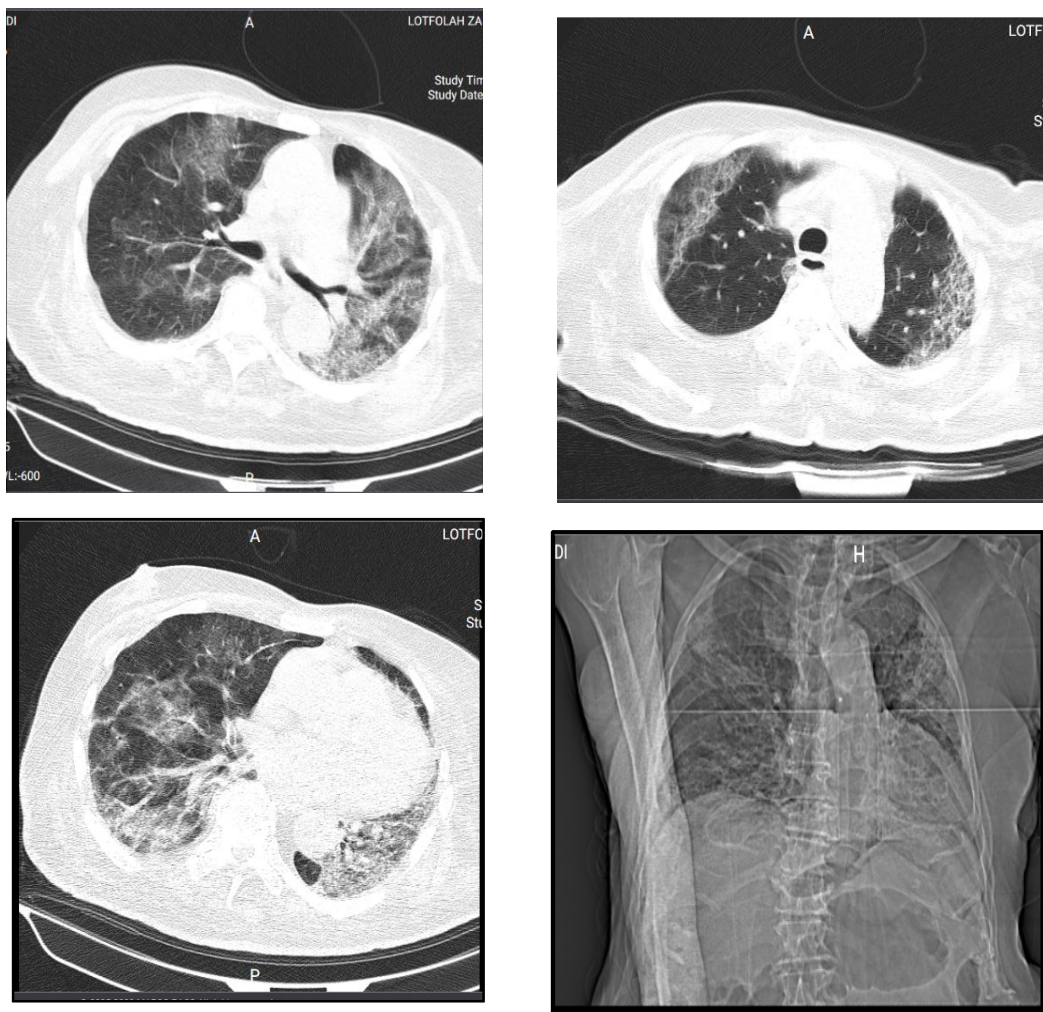


Fig 1. Chest CT scan showing bilateral ground-glass opacities with consolidation and mediastinal lymphadenopathies in aortopulmonary window

On physical examination his blood pressure was 148/84, body temperature was 37.7°C and oxygen saturation was 88% on room air.

Lab tests on first day of admission revealed elevated WBC at $26 \times 10^3/\mu\text{L}$ and lymphocyte at $16 \times 10^3/\mu\text{L}$.

Hemoglobin, platelet, CRP, troponin and LDH level were 14.7 g/dl, $301 \times 10^3/\mu\text{L}$, 18mg/L, 42ng/l and 755u/l, respectively. On day 10, WBC and lymphocyte count increased to $38.7 \times 10^3/\mu\text{L}$ and $23.6 \times 10^3/\mu\text{L}$, respectively (Figure 2).

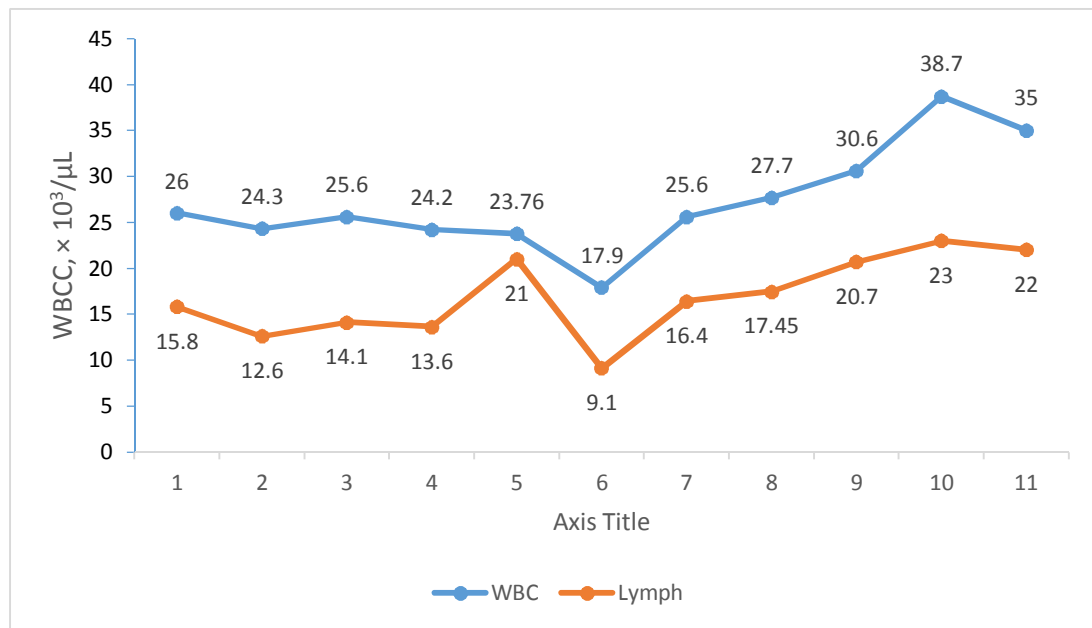


Fig 2. White Blood Cell (WBC) Count and Lymphocyte (Lymph) Count Changes during 10 Days Hospitalization

He received dexamethasone (8 mg per day), daclatasvir/sofosbuvir (60/400mg per day), meropenem (1gr twice a day), levofloxacin (500 mg per day) and interferon beta 1-alpha (44 ug every other day). The patient also received preventive doses of PPI, anti-coagulation, vitamin C, vitamin D, and zinc.

Peripheral blood smear showed proliferation of small mature lymphocytes with the presence of smudge and basket cells (Figure 3). Immunophenotype assay characterized by monoclonal B cells ($\text{CD}20^+$ & $\text{CD}19^+$) with co-expression of $\text{CD}5$ & $\text{CD}23$ confirmed the diagnosis of CLL.

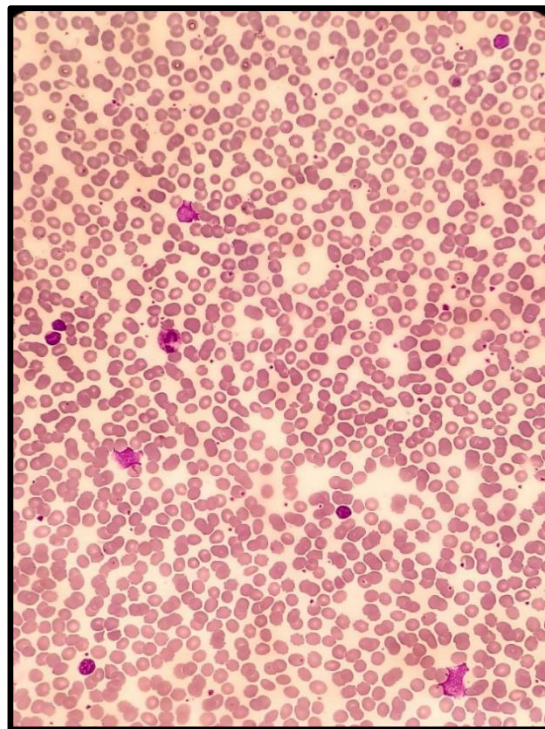


Fig 3. Proliferation of small mature lymphocytes with presence of smudge and Basket cells, which are most often associated with abnormally *fragile lymphocytes* in disorders such as chronic *lymphocytic leukemia (CLL)*

After 11 days, the symptoms were alleviated, patient was conscious, shortness of breath subsided, oxygen saturation increased to 95% and he was discharged to home isolation.

This case report was approved by the Iran University of Medical science ethical board and informed consent was obtained from the patient.

CLL is the most common leukemia in adults. Patients are often asymptomatic and about one third of them do not require treatment (4). At the time of diagnosis, patients often have normal hemoglobin and platelet counts and have elevated white blood cell count with an absolute lymphocytosis (lymphocyte count $>5.0 \times 10^9/\text{liter}$).

In peripheral blood smear, “smudge cells” (nonintact white blood cells) and a population of small to medium-sized lymphocytes with a mature and clumped chromatin pattern nucleus are observed (5).

Flow cytometry on peripheral blood diagnosis of chronic lymphocytic leukemia. The lymphocytes have a characteristic immunophenotype: monoclonal B cells that co-express CD5 and CD23 and are usually negative for FMC 7(6).

COVID-19 seems to be more severe in CLL patients than in the general population, and CLL patients have worse outcomes, and higher mortality ranging from 11.4% to 35.5% compared to general population with 3% mortality(7).

In contrast to leukocytosis, lymphopenia is a common laboratory finding in patients with COVID-19 and is a poor prognostic factor in patients with severe disease (8, 9). Liu et al. found that lymphocyte count decrease in initial phase of COVID-19, then gradually increase from day 7 to 15 after disease onset (10).

Our case, presented with lymphocytosis and had a 1.5-fold increment of lymphocyte count during hospitalization (11). A recent study by Paneesha et al.(12) Investigated 4 patients with treatment-naïve CLL with severe COVID-19 infection. The average peak lymphocytosis in all patients was 3-fold higher than the most recent outpatient appointment. The investigators described this phenomenon as “COVID-19–induced lymphocytosis.”

The mechanism of COVID-19-induced lymphocytosis in CLL is unknown. It may be caused by high levels of endogenous steroids during severe inflammation, but additional mechanisms may be in operation and further investigation is needed. It is unknown whether a sudden increase in the lymphocyte count can be used as a prognostic factor in patients with treatment-naïve CLL and acute COVID-19 infection (12).

Also, the outcomes of all patients with treatment-naïve CLL are not similar. A report by Baumann et al. (13) described 4 patients with CLL and acute COVID-19 infection. Two of them had never received any treatment for their CLL and recovered from their acute COVID-19 infection. Similarly, in our study, the patient recovered and discharged despite the increase in the lymphocyte count.

There is a challenge in treatment of patients with CLL and COVID-19. It seems that the immune system in CLL patients is not efficient and lymphocytes do not respond strongly to the viral infection. It might help to prevent excess cytokine release, the subsequent damage and multi-organ involvement in CLL patients. So, this could be a protective factor against a severe COVID-19 infection (14).

Nevertheless, chemotherapy is controversial in CLL and COVID-19 patients. It can worsen SARS-COV-2 immunodeficiency, lead to cardiotoxicity and worsen the prognosis. Chemotherapy should be avoided for CLL patients presenting COVID-19 to restrain treatment-related immunodeficiency and prevent drug interactions (15).

Further surveys should be planned to assure an optimal approach to the management of patients with CLL during the COVID-19 pandemic.

Conclusion

Hematologic malignancies such as CLL can mask clinical and biological symptoms of COVID-19 such as lymphopenia. Lymphocytosis is an unexpected finding in COVID-19 patients, and an increase in lymphocytes may indicate other conditions. In these cases, secondary causes of lymphocytosis, such as malignancy or other

infections, should be considered. Treatment should be personalized according to the status of the patient's immune response and comorbidities.

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Conflict of interest

The authors have no conflict of interest in this study.

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