

COVID-19 with Rapidly Progressive course in a Patient with CD5 Negative Chronic Lymphocytic Leukemia

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Abstract

Limited data are currently available on the clinical course of COVID-19 patients with chronic lymphocytic leukemia (CLL). B cells in chronic lymphocytic leukaemia (CLL) usually express the CD5 antigen, which appears to participate in the pathogenesis of autoimmune phenomena. However, 7-20% of B-CLL patients are CD5-. Studies of CD5- patients without COVID-19 seemingly present with milder disease and have a favourable prognosis compared with the vast majority of B-CLL patients who express CD5. When the course of CD5- CLL patients is complicated by COVID-19, the prognosis may not however be as predictable. We present a 50-year-old male with CD5- CLL, who developed COVID-19 and died shortly after a severe and rapidly progressive course. It is therefore important to educate these patients on the necessity of being vaccinated against COVID-19 and when infected, treated early and aggressively with the available antiviral therapies.

INTRODUCTION

Adult patients with hematologic malignancy and COVID-19, especially hospitalized patients, have a high risk of dying.

Patients ≥ 60 years have significantly higher mortality; pediatric patients appear to be relatively spared. An intact immune response is needed to face the initial infection and clear the virus, with patients recovering from the infection demonstrating evidence of humoral neutralizing antibodies¹(Rongqing et al., 2020). The severity of COVID-19 and multi-organ failure (MOF) occurrence seem to be related to clinical and laboratory parameters of inflammatory response (lymphopenia, hypoalbuminemia, higher levels of alanine aminotransferase, lactate dehydrogenase, C-reactive protein, ferritin, and D-dimer) and markedly higher levels of proinflammatory cytokines (interleukin-2 receptor, IL6, IL-10, and tumor necrosis factor γ)²(Chen et al., 2020). On these grounds, therapies targeting inflammation (e.g., IL6/IL6R antibodies or steroids) have been used and shown potential benefit in full-blown COVID-19 patients³(England et al., 2021). When severe COVID-19 occurs, it is probably the underlying leukemic disease with the typical immune dysregulation that predisposes to a dismal outcome, levelling off the death risk and overcoming the effect of age and other comorbidities(Scarfò et al., 2020). It is estimated that 7-20%

of CLL patients are CD5 negative, but the cell marker's role in prognosis is yet to be determined. The current evidence on clinical differences and prognosis of CD5 positive patients compared to CD5 negative patients is controversial (Demir et al., 2017). We present a case of CD5 negative CLL with rapidly progressive course that culminated in patient's demise.

CASE REPORT

A 50-year-old male with past medical history of hypertension and type II diabetes mellitus was brought to the emergency department by paramedics complaining of progressively worsening shortness of breath of two weeks duration. The patient had tested positive for COVID-19 one month earlier and was admitted to another hospital a few days earlier with dyspnea and placed on oxygen, but decided to leave against medical advice. History of present illness revealed known sick contact for COVID19. Vitals signs included a temperature of 98.2°F, pulse of 105/min, and respiratory rate of 45/min. An admitting chest x-ray revealed diffuse patchy bilateral opacities scattered throughout both lungs, resembling a multifocal pneumonia. CT pulmonary angiogram with contrast showed extensive bilateral ground-glass opacities, enlarged mediastinal lymphadenopathy, and mild splenomegaly without evidence of pulmonary embolism. Admitting serologic tests for SARS-CoV-2: RNA

(RT-PCR), IgG AB, and IgM AB were all positive. He was diagnosed with COVID-19 pneumonia. He was at that time on 6 liters of 100% oxygen.

Significant laboratory findings included: marked leukocytosis (97.4/μL) with 56% lymphocytes; hypoalbuminemia (1.2 g/dL); hyperkalemia (6.8 mmol/L); BUN, 54 mg/dL; creatinine, 1.44 mg/dL; C-reactive protein, 15.60 mg/d; and alkaline phosphatase, 698 IU/L. Serum protein electrophoresis was positive for an elevated monoclonal gamma globulin spike. Arterial blood gases included the following abnormal findings: PCO₂, 84.4 mmHg; HCO₃, 19.5 mEq/L; pH, 6.98; and PO₂, 112.1 mmHg.

A peripheral smear preparation showed conspicuous lymphocytosis, consisting of mature lymphocytes with occasional cleaved nuclei and smudge cells (Figures 1 and 2). Flow cytometry of the peripheral blood showed monoclonal B-cells with co-expression of CD19, CD20, and CD23 but negative for CD5 and CD38, consistent with a CD5 negative CLL.

During hospitalization, the patient developed asystole with progression to cardiac arrest and expired five days following his latest hospital admission.

Figure 1

Peripheral smear shows lymphocytosis, consisting of abnormal mature lymphocytes. A neutrophil is present in center of the image.

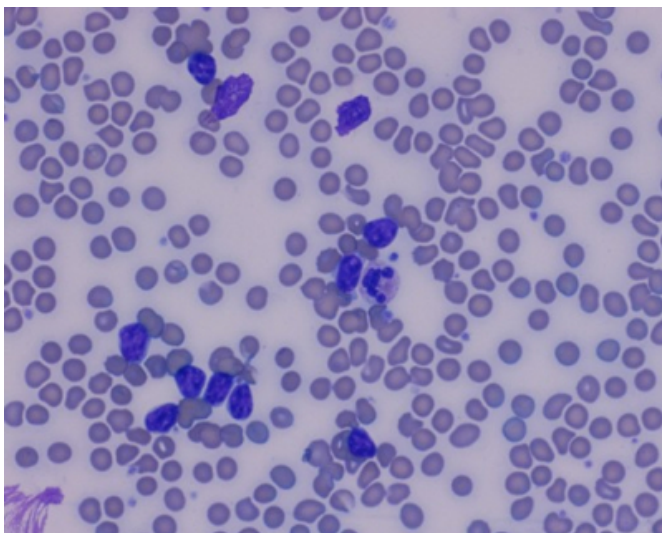
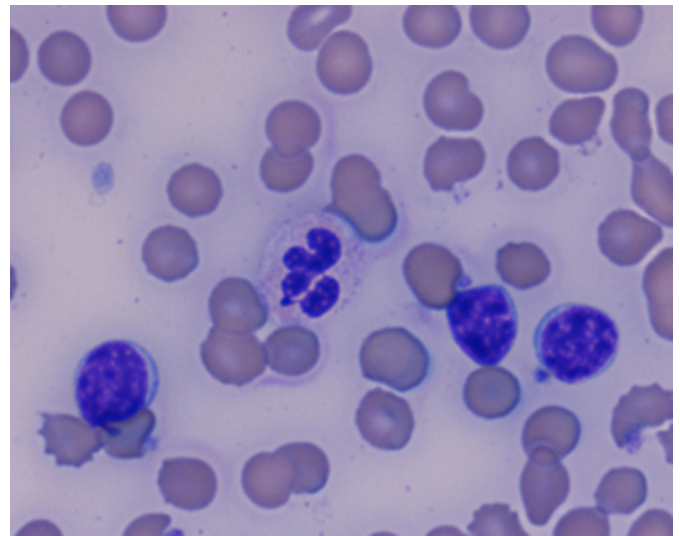


Figure 2

High-power view of the peripheral smear shows presence of mature lymphocytes, one with cleaved nucleus and a neutrophil.



DISCUSSION

In light of the recent SARS-CoV-2 (COVID19) pandemic, cancer patients were shown to be at 3.5 times higher risk of admission to ICU and mechanically ventilated (Liang et al., 2020). The average age of patients infected by the COVID19 virus is 56 years, and males appear to be affected more. Comorbidities like hypertension, diabetic cardiovascular disease and chronic illness are factors of susceptibility, leading to poorer prognosis and outcomes (Richardson et al., 2020).

Chronic lymphocytic leukemia (CLL), the most common leukemia in adults, is characterized by clone of B cells with the co-expression of CD19, CD20, CD5, and CD23. It is estimated that 7-20% of CLL patients are CD5 negative, but the cell marker's role in prognosis is yet to be determined. CD5, specifically is thought to be a negative regulator of B cell signaling, and its absence enhances proliferation of B cells, by decreasing apoptosis (Burgueño-Bucio et al., 2019). Various studies found greater incidence of splenomegaly in CD5 negative CLL patients, less lymphadenopathy, greater leukocytosis and thrombocytopenia, but no difference in survival compared to patients with CD5 positive CLL (Demir et al., 2017). Yet, a case-control study with 29 CD5 negative CLL patients concluded that prognosis is more favorable in the absence of CD5 (S et al., 2002). Thus, the current evidence on clinical differences and prognosis of CD5 positive patients compared to CD5 negative patients is controversial.

COVID19 infection involves a rapid viral replication that needs to be controlled by the immune system, if it is not controlled a cytokine-induced inflammatory storm is initiated and severe pulmonary disease can occur. Patients with CLL have a weakened immune system and impaired innate immunity responses, which could make it harder to clear the virus and possibly increase risk of infection.

A European international multicenter study on COVID19 found that 88.9% of the patients with CLL studied required hospitalization (Scarfò et al., 2020). A meta-analysis of 3377 patients with hematologic malignancies and COVID19, showed that risk of death was 34% (Vijenthira et al., 2020) and it was slightly less at 31% for patients with CLL, specifically (Riches, 2021).

In this case report, we have presented a patient diagnosed with severe COVID19 pneumonia found to have coincidental CD5 negative CLL with a rapidly progressive course of the disease. Additional studies may be necessary to understand the prognostic implication of CD5- CLL patients with viral infections such as Covid 19 and approach to treatment of such unique binary presentations.

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