



Chronic lymphocytic leukemia

CLL and COVID-19 at the Hospital Clinic of Barcelona: an interim report

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To the Editor:

COVID-19 caused by SARS-CoV-2 has led to a global pandemic already affecting over 3.5 million persons with more than 243,000 confirmed deaths [1]. Early reports from China indicate that persons with cancer are more susceptible to SARS-CoV-2 [2]. However, there are no data on the prevalence of COVID-19 in different types of cancer, including chronic lymphocytic leukemia (CLL).

CLL is the most frequent leukemia in Western countries with an incidence of 4.2:100,000/year, increasing to more than 30:100,000/year at an age of >80 years. The median age at diagnosis is 72 years, and most patients are older than 60 years. Data from US SEER estimated >20,000 newly diagnosed cases of CLL in 2019 [3]. CLL is frequently accompanied by immunodeficiency (that can be aggravated by therapy) and comorbidity. Infections are the first cause of death in CLL. Cancer, older age, immunodeficiency, and chronic diseases are all risk factors for COVID-19 [4]. It could be hypothesized, therefore, that patients with CLL are among those with a higher risk to contract COVID-19. However, the prevalence, clinical characteristics, and outcome of patients with CLL and COVID-19 infection have not yet been established, and to obtain the full picture will take time. Meanwhile, preliminary information from large series of patients can be useful.

The Hospital Clinic from Barcelona is a reference center for CLL. In the period 2000–2019, 804 patients with CLL were registered. The median age was 67 years. The median overall survival is 11.8 years. Three hundred and eighty-four patients have died; in 236 with available information, infection was the cause of death in 35% subjects. The

median follow-up of 420 patients who remain alive is 7.9 years. Four of these patients (0.95%) have been diagnosed with symptomatic COVID-19. Their characteristics and outcome are shown in the Table 1. Of note, the number of patients with COVID-19 admitted at the Hospital Clinic of Barcelona as of 6 May 2020 is 2366.

All four patients were males, old and suffered from comorbidity; three had increased ferritin levels; two presented lymphocytopenia; and one had increased D-dimer levels, all features associated with poor outcome in COVID-19 [4]. Also, two patients had previously received therapy for CLL. Despite this, the course of the disease was mild, and no patient required admission in an intensive care unit; three patients quickly recovered after 4–8 days and one after 24 days of experimental therapy for COVID-19. It could be speculated that the CLL-related immunodeficiency, rather than exacerbating the effects of SARS-Cov-2 might prevent them [5]. This, as well as the potential role of immunomodulatory agents (e.g., ibrutinib) on the outcome of patients with CLL infected by SARS-Cov-2, deserves investigation [6, 7].

The concept that patients with cancer have a high-risk for COVID-19 derives from reports describing the underlying conditions in patients with COVID-19 [8, 9]. Ours is the first attempt to directly determining the prevalence of COVID-19 in CLL. In short, 4 of 420 (0.95%) patients, representative of the general CLL population, have been so far diagnosed with mild, symptomatic COVID-19. The seemingly low prevalence of symptomatic COVID-19 in CLL needs to be taken cautiously as the number of cases may increase as long as the pandemic persists. Several recently launched studies, will help to clarify the prevalence of COVID-19 in CLL, its clinical characteristics, optimal therapy, and outcome. Meanwhile, this interim report based on a large series of patients provides a frame to gauge the likely impact of COVID-19 on patients with CLL. Also, different organisms have issued helpful recommendations on the prevention of COVID-19 in patients with CLL or cancer in this dramatic and challenging moment [10, 11].

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Table 1 Main characteristics of patients, treatment, and outcome.

	Male, 72 years old CLL, A0, del13q/ HCL Previously treated	Male, 75 years old CLL, A0, trisomy 12 Never treated	Male, 80 years old SLL/CLL, del13q Previously treated	Male, 75 years old CLL, AI, del11q, del13q Never treated
Comorbidity	Malignant melanoma and basal cell carcinoma of the skin (surgical treatment)	Sleep apnea, diverticulitis	Squamous carcinoma in tonsillar fossa. Treated with cetuximab and radiotherapy in 2017	Coronary heart disease, hypertension, basal cell carcinoma of the skin
Symptoms	Fever (24 h) and diarrhea (4 days). No respiratory symptoms, SpO ₂ : 96%	Fever and malaise (7 days). No respiratory symptoms, SpO ₂ : 96%	Fever and dry cough (24 h). Slight shortness of breath, SpO ₂ : 95%	Fever and dry cough (24 h). SpO ₂ : 98%
Chest X-ray/ CT scan	Slight lower right lung infiltrate	Upper left lung infiltrate	Bilateral interstitial infiltrate	Bilateral interstitial infiltrate
WBC (×10⁹/L)	3.5	16.95	2.4	56.9
ALC (×10⁹/L)	0.35	13	0.3	50.1
Hb (g/L)	138	139	131	119
Platelets (×10⁹/L)	76	77	163	163
CRP (mg/dL) (N <1)	4.8	0.4	16	7.7
Procalcitonin (ng/ml) (N <0.5)	0.48	0.05	0.07	0.57
LDH (U/L) (N <234)	282	232	304	199
Ferritin (ng/mL) (N <400)	776	487	997	167
D-Dimer (ng/mL) (N <500)	500	900	400	300
Troponin I (ng/L) (N <45)	3.0	4.9	6.3	7.7
Treatment	Lopinavir/ritonavir oral (4 days) Hydroxychloroquine oral (4 days) Azithromycin (4 days)	Lopinavir/ritonavir oral (7 days) Hydroxychloroquine oral (5 days) Azithromycin oral (5 days)	Ceftriaxone iv (4 days) Teicoplanin iv (4 days) Lopinavir/ritonavir oral (7 days) Hydroxychloroquine oral (5 days) Azithromycin oral (5 days)	Ceftriaxone iv (2 days) Teicoplanin iv (2 days) Lopinavir/ritonavir oral (2 days) Hydroxychloroquine oral (2 days) Azithromycin oral (2 days)
Outcome	Recovery. Referred (day 4) to ambulatory care program	Recovery. Referred (day 8) to ambulatory care program	Recovery. Referred (day 8) to ambulatory care program	Recovery. Referred (day 24) to ambulatory care program

COVID-19 preventive measures as per the Spanish Health System and Ad hoc Hospital Clinic of Barcelona Recommendations. Diagnosis by RT-PCR. ALC absolute blood lymphocyte count, CR complete response, HCL hairy-cell leukemia, PR partial response.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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