Covid-19 in patients with chronic lymphocytic leukemia: Clinical outcome and B- and T-cell immunity during 13 months in consecutive patients

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INTRODUCTION

- Patients with CLL have an increased risk of severe infections due to disease- and treatment related immunodeficiency.
- During the Covid-19 pandemic early international surveys reported a high fatality rate among CLL patients admitted to hospital due to severe Covid-19.
- Also, CLL patients might not respond due to severe Covid-19.
- We report on the clinical and immunological outcome of Covid-19 in consecutive patients with CLL from a well-defined area during the first 13 months of the pandemic.

Objectives

- To investigate hospitalization, ICU-admission and fatality rates during months 1-4 vs month 7-13 of the pandemic, and identify possible prognostic factors.
- To investigate B- and T cell immunity during long-term follow-up.

METHOD

- Patients with CLL at three hematology centers in Stockholm (covering >95% of patients with CLL in the region) who had a history of PCR-confirmed, symptomatic Covid-19 during March 1-2020 until March 31-2021 were included (n=60).
- Baseline clinical characteristics included age, gender, CIRS, CLL treatment history, CLL status, blood counts and Ig levels.
- Data was also collected on Covid symptoms, hospitalization/ICU admittance and its length, Covid-19 treatment and clinical outcome.
- Convalescent blood samples were obtained from most survivors at 3-6 months and up to 12 months post infection and analyzed for SARS-CoV-2 antibodies.
- In depth immunological analyses was performed in a subset of convalescents and included whether antibodies had neutralizing capacity (competitive bead-based binding assay), if SARS-CoV-2 specific antibodies could be found in saliva (self sampling kit) and whether T-cell specific response occurred (IFN-gamma ELISpot assay).

RESULTS

- Baseline characteristics and clinical outcome
  - 60 patients were included with a median age of 71 years, median CIRS 8, median BMI 25, and 65% were men.
  - Patients had indolent CLL (n=38), were previously treated (n=12, all >12 months ago) and had ongoing therapy (n=10, among which 7 received BTKi).
  - 46 patients (77%) were hospitalized due to severe Covid-19, of these 11 (24%) were admitted to ICU.
  - Severe Covid-19 was equally distributed across subgroups irrespective of gender, age, BCL status and CLL treatment except CIRS (p<0.05).
  - 14 patients (23%) died; age 72 years was the only significant risk factor (p<0.05, multivariate analysis).
  - Outcome month 1-6 vs 7-13 and Covid management
  - ICU admission and death rates were numerically reduced in the second time period (37% to 15% and 32% to 18%, respectively) while hospital admission remained frequent (86% vs 71%).
  - 85% of admitted patients needed supplemental oxygen (both time periods).
  - There was a numerical increase in the use of remdesivir in the second time period (5% vs 41%).
  - Corticosteroids became more widely applied during month 7-13 of the pandemic (from 47% to 78%).

- Immunological results
  - Seroconversion occurred in 34/41 (83%) of convalescents and anti-SARS-CoV-2 antibodies remained detectable at 6 and 12 months in follow-up in 17/22 and 11 patients, respectively.
  - Immunological analyzes also revealed that 13/17 tested patients had neutralizing antibodies (of which 1 patient was negative in conventional serology).
  - 19/28 patients (68%) had SARS-CoV-2 specific antibodies in saliva.
  - SARS-CoV-2 specific T-cells were detected in 14/17 patients (82%) and was generally paralleled by seroconversion.

CONCLUSIONS

- Covid-19 continued to result in high admission and fatality rates even among consecutive and young early-stage CLL treatment.
- The only significant risk factor of death was age ≥75 years.
- Risk of death and ICU admission declined in the second time period.
- A robust and durable B- and/or T-cell immunity was observed in most convalescents.