Transient disappearance of CD19+/CD5+ B-Lymphocytes in peripheral blood in a patient with CLL during SARS-CoV-2 related mild disease

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Abstract

We report a 64-years old man with B-cell CLL infected by SARS-CoV-2 during his hospitalization for a spondylodiscitis. Because of his health conditions the duration of the antiviral therapy was restricted to one week where we observed a transient disappearance of CD19+/CD5+ B-lymphocytes in peripheral blood.

Title

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Authors

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KEYWORDS

SARS-CoV-2, lymphocytic leukaemia, CD19+ cells, CD5+ cells

KEY CLINICAL MESSAGE

The negative outcome COVID-19 in patients with malignant diseases calls to specific actions for the clinical and diagnostic management of new coronavirus infection, especially in blood cancer, where viral clearance can be dramatically slow.

INTRODUCTION

Currently, coronavirus disease 2019 pandemic caused more than one million of deaths worldwide, with more than 54 million of confirmed cases in less than one year. Individuals with malignancies are considered high risk patients for bacterial, fungal, and viral infections.

To date a few data are available on the real incidence and outcome of COVID-19 in patient with chronic lymphocytic leukaemia[1,2]. An Italian survey involving 33 haematology centres with at least 100 patients per centres and involving 9930 CLL patients showed that less than 0.5% (47/9930) were found positive to COVID-19 [3].

CASE PRESENTATION

Here we describe a case of a SARS-CoV-2 positive patient with chronic lymphocytic leukaemia (CLL) and other comorbidities. Although was efficaciously treated, and IgG seroconverted, the patient remains SARS-CoV-2 positive two months after the disappearance of the symptoms. Moreover, the strong leucocytosis observed before the infection is dramatically reduced so that the leukocyte count is, to date, stably within the reference range. We had the opportunity to follow the time-course of biochemical, haematological, and coagulative indexes before, during and after the infection. On February 26, 2020, a 64-years-old man with a clinical history of chronic monoclonal B lymphocytes lymphocytic leukaemia (immunophenotype CD19+, CD5+, CD22+, CD23+, CD103 neg, FMC7 neg), type II diabetes, high blood pressure and vertebral instability was admitted at the Regional Hospital "San Salvatore" of L'Aquila, Italy for the acute exacerbation of the lumbosacral pain. The patient refers nausea, body temperature above 38°C, dysuria, and strangury. At admission, the haematological parameters were coherent with his previously diagnosed CLL: leukocytes were $18.33\times10^3/\mu L$ with lymphocytes and neutrophils representing 56.5% and 40.1% of total white blood cell count, respectively. The most relevant biochemical parameters included glycemia (145 mg/dL) coherent with type II diabetes, and C-reactive Protein (CRP) which was significantly elevated (18.73 mg/dL) as well as the erythrocyte sedimentation rate (120 mm/h). Other clinical parameters including estimated glomerular filtration rate, serum electrolytes, cardiac, muscle, pancreatic and liver enzymes were normal, except for gamma-glutamyltransferase which was slightly elevated (72 UI/L). Coagulative indexes and plasma brain natriuretic peptide were normal.

The NMR of the lumbosacral rachis was compatible with a suspected spondylodiscitis, although the microbiological analysis of the biopsied sample obtained from the L4-L5 intervertebral disc was negative as well as, urine, blood, and faeces. Chest X-rays did not show alterations of lungs. The patient was treated with levofloxacin (750 mg) and teicoplanin (400 mg) once a day for 4 weeks, pregabalin 75 mg, oxycodone/naloxone 5/2.5 mg and tramadol/paracetamol 37.5/325 mg were orally administered once a day for pain relief, metformin 500 mg twice a day for glycaemic control, and the ACE2 inhibitor ramipril 2.5 mg for hypertension. The patient was moved from the Internal Medicine ward to the Long-term care ward the 10^{th} of March with CRP 0.7 mg/dL and unaltered haematological parameters. The 18^{th} of March, following possible exposure to a symptomatic COVID-19 positive roommate, the patient was found COVID-19 at real time RT-PCR assay and immediately transferred to Infectious Disease ward. The real time RT-PCR assay of the nasopharyngeal swab resulted positive to SARS-CoV-2 with no related symptoms although CRP immediately increased to 4.32 mg/dL and leukocytes count dropped to $5.79\times10^3/\mu L$. The 23^{rd} of March arterial oxygen saturation (SaO_2) was around 90% and CT scan of the chest showed bilateral ground-glass opacities, prevalently peripheric, compatible with new coronavirus infection. CRP and ferritin rapidly increased to reach the maximum 3 days after, 11.89 mg/dL and 1695.6 mg/dL, respectively. The increase of the inflammatory markers was anticipated by marked reduction in leukocytes and lymphocytes counts, whose values were perfectly within the reference ranges during the infection; the inverted leukocyte formula (neutrophils 30.6%, lymphocytes 64.8%) at the 5^{th} of March, became normal during the active infection (neutrophils 58.5%, lymphocytes

37.2%) (figure 1).

He was successfully treated with darunavir (800 mg), ritonavir (100 mg) once a day and hydroxychloroquine (200 mg) twice per day for one week. CRP and ferritin return within the reference ranges and no other biochemical alterations were observed. To date, three months after COVID-19 infection, the patient is still positive to real time RT-PCR assay. He is completely asymptomatic and biochemical and coagulative indexes, as well as arterial blood gas test, are within the reference ranges. The patient developed humoral immunity with a strong anti-SARS-CoV2 IgG response, but not IgM, presumably due to the low titre at the time of the analysis executed 45 days after the COVID-19 diagnoses. However, negativity to IgM has been described in recent study, suggesting the possibility of a uncomplete seroconversion in CLL patients [4]

Mean haematological parameters calculated in the last two months are, despite the previously diagnosed CLL, characterized by normal leukocytes count ($8.64\pm0.36\times10^3/\mu L$), normal neutrophils count ($3.09\pm0.20\times10^3/\mu L$) and a moderate lymphocytosis ($5.02\pm0.46\times10^3/\mu L$), resulting in an inverted leukocyte formula (neutrophils 58.13±3.08%, lymphocytes 35.86±3.10%).

DISCUSSION

In this report we discussed the clinical outcome of a patient with untreated CLL and other comorbidities which are considered to increase the mortality in COVID-19 infection. In Italy, the most common comorbidities observed in COVID-19 positive deceased patients are hypertension (73.8%), and diabetes (33.9%) (Characteristics of COVID-19 patients dying in Italy. Report based on available data on March 20th, 2020, National Institute of Health,*https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-analysis-of-deaths*). The patient was empirically treated since no recommendations about the management of lymphoid malignancies were available at that time. Actually several guidelines about the management of lymphoid malignancies have reported [5,6].

In our opinion, the reported case represents an unexpected result since there is great concern about the potential negative outcome in SARS-CoV-2 infection in patients with malignant diseases. Moreover, the leukemic CD19+/CD5+ clone, disappeared from peripheral blood during acute phase of COVID 19, recovered in convalescent phase of disease.

CONCLUSION

Although it cannot be possible to generalize looking to a specific case, the absence of viral titre negativization in the last two months in a B-cell CLL patient calls to specific actions for the clinical and diagnostic management of new coronavirus infection in patient with blood cancer. Informed consent from the patient has been acquired.

AUTHOR CONTRIBUTION

RB, GDM and AC were involved in data collection. PB and AP were involved in data analysis and interpretation. MP and GA critically revised the manuscript. GC wrote the manuscript.

DECLARATION OF INTERESTS

Nothing to declare

ABSTRACT

We report a 64-years old man with B-cell CLL infected by SARS-CoV-2 during his hospitalization for a spondylodiscitis. Because of his health conditions the duration of the antiviral therapy was restricted to one week where we observed a transient disappearance of CD19+/CD5+ B-lymphocytes in peripheral blood.

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Figures

Figure 1 . Aligned time-course plots of significative haematological parameters (leukocytes count and lymphocytes percentage) and inflammation markers (C-reactive protein and ferritin) recorded from the 26^{th} of February 2020. Real time RT-PCR diagnoses of COVID-19 infection was the 18^{th} of February. Dashed lines represent the upper limit of the reference ranges.