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LETTER TO THE EDITOR

Seroconversion and kinetic of anti SARS-COV-2 antibodies in 25 patients with hematological malignancies who recovered from SARS-COV-2 infection

Data on the dynamics and duration of humoral immune responses against SARS-CoV-2 in hematological patients are still lacking. Preliminary studies in non-immunocompromised subjects with COVID-19 reported seroconversion 7 to 14 days following symptom onset, with increased IgM and IgG titers observed during the first month. IgM levels, after peaking by day 30, gradually decreased and were undetectable by day 180. The long-lasting persistence of IgG has not been clearly demonstrated.[1–5]

We evaluated the humoral response and kinetics of IgM and IgG against SARS-CoV-2 in 25 hematologic patients, receiving anticancer therapy, who were followed after real-time quantitative polymerase chain reaction (RT-qPCR) confirmation of SARS-CoV-2 infection. The patient demographics and clinical characteristics are shown in Table 1. The median age was 59 years (range 21–85). The underling hematologic diseases were: lymphoma (10/25), myeloma (7/25), chronic lymphoproliferative diseases (5/25) and acute leukemia (3/25). SARS-CoV-2 infection was mild symptomatic in 5/25 (20%) cases and symptomatic in 20/25 (80%), the most frequent symptoms being fever, sore throat, anosmia, cough, shortness of breathing, and fatigue. Four of the 20 symptomatic patients had pneumonia requiring hospitalization. None of these 25 patients died from COVID-19.

The median IgG, IgM, and IgA values at SARS-CoV-2 infection onset were 832 mg/dl (167–2210 mg/dl), 54.5 mg/dl (6–2510 mg/dl), and 54 mg/dl (8–605 mg/dl), respectively. The median lymphocyte count was 1100/mmc (250–3300/mmc).

The IgM and IgG antibodies against SARS-CoV-2 spike protein (subunity S1 and S2) were tested by chemiluminescence immunoassay (CLIA) with a positive cut-off value of 12 UA/ml for both IgG and IgM. The specificity and sensibility of this assay was 98,5% and 97,4%, respectively.[6] All patients signed written informed consent for the serological test. To assess the kinetics of antibody titers, in our convalescent COVID-19 patients, serum IgM and IgG levels were longitudinally measured at established time points: 1 month (T1) 2 months (T2), 3 months (T3), 4 months (T4) and 6 months (T6) after their first positive nasopharyngeal swab test. None of these cases received anti SARS-CoV-2 vaccination during the study period.

Among these 25 confirmed COVID-19 cases, 21/25 (84%) developed specific anti SARS-CoV-2 antibodies with a titer > 12 UA/ml in almost one of the specific time points. However, as reported in Figure 1 (A) and 1(B), after a peak of the IgG and an overall mild increase of IgM, the antibody titer declined from 4 months after the disease onset under the positive cut-off value, although variation between patients was detected. The mean and median titers were detailed in Figure 1(A) and 1(B).

TABLE 1 Characteristics of 25 Hematologic patients with COVID-19

No. of cases	25
Sex (M/F)	12/13
Median age-years (range)	59 (21–85)
Hematologic malignancies	
• Lymphoma	10/25 (40%)
• Myeloma	7/25 (28%)
• Chronic lymphoid leukemia (CLL)	5/25 (20%)
• Acute leukemia	3/25 (12%)
Concomitant therapy	
• Chemotherapy (CHT)	10/25 (40%)
• Steroids	5/25 (20%)
• Rituximab ± CHT	4/25 (16%)
• Daratumomab ± CHT	4/25 (16%)
• Ibrutinib or venetoclax	3/25 (12%)
• Other[a]	2/25 (8%)
Immunoglobulins,[b] mg/dl- median (range)	
• IgG	832 (167–2210)
• IgM	54,5 (6–2510)
• IgA	54 (8–605)
Lymphocytes[b], N/mmc-median (range)	1100 (250–3300)

[a]1 Nivolumab; 1 Ponatinib and prednisone.
[b]Median values at SARS-CoV-2 infection onset.

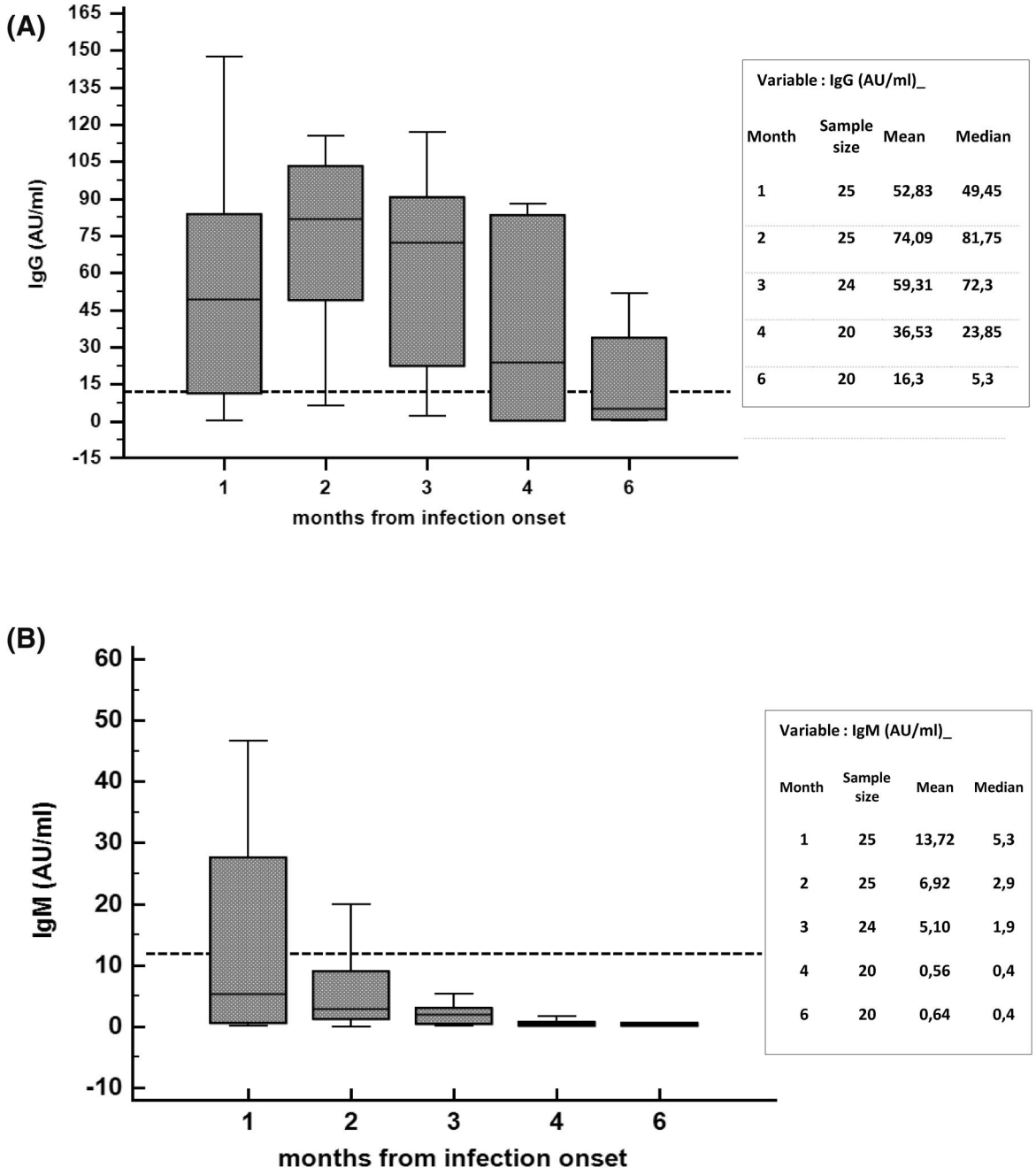

FIGURE 1 Determination of IgG (A) and IgM (1B) antibody levels against SARS-CoV-2 at different time points from SARS-CoV-2 infection onset. Horizontal dot line represents positive cut-off value (12 UA/ml)

In summary, although we analyzed a limited number of cases, patients with hematological malignancy appear to have an antibody response to SARS-CoV-2 and a high rate of seroconversion (84%). However, the kinetic of antibody levels may suggest that the duration of antibody-mediated protection against re-infection with SARS-CoV-2 may be short-lasting.[7,8] If confirmed in a larger number of cases, these findings would suggest that stringent infection prevention and control measures must be maintained in hematological patients who have recovered from COVID-19. In addition, our results would suggest that hematological patients could require a periodic re-vaccination. Obviously, additional studies of both humoral and cellular immunity (T and memory B cells) will be necessary to better understand the dynamics, duration, and intensity of the overall immunological response to SARS-CoV-2 infection in hematological malignancy patients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Anna Candoni performed the research, collected the data and wrote the letter. Umberto Pizzano collected the data, Martina Fabris

performed the quantitative serological test. Francesco Curcio and Renato Fanin revised the letter. All the authors approved the final version.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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