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mRNA COVID-19 Vaccination in Active COVID-19—Infected Acute Myeloid Leukemia Patient

To the Editor:

We present a case of a 64-year-old Chinese female with intermediate risk acute myeloid leukemia (with t(9;11) (p21.3;q23.3); KMT2A–MLLT3, who had undergone induction chemotherapy with a continuous infusion of standard-dose cytarabine 100 mg/m² for 7 days with daunorubicin 60 mg/m² for 3 days (DA60 3+7). Following her induction, she achieved morphological remission with evidence of minimal residual disease on flow cytometry. As she declined allogenic stem cell transplant postinduction therapy, she continued with 1 cycle of continuous infusion standard-dose cytarabine 100 mg/m² for 7 days with daunorubicin 45 mg/m² for 3 days (DA45 3+7) and 2 cycles of intermediate-dose cytarabine with daunorubicin (MODAC).

During her admission for planned 2nd cycle of MODAC, she was found to have persistent neutropenia with nonproductive cough and fever. Nasal swabs were positive for both human coronavirus 229E (HCoV 229E) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Chemotherapy was then postponed due to coronavirus disease 2019 (COVID-19) infection. Patient also had not received prior COVID-19 vaccination. Initial chest radiographs showed few faint patchy airspace opacities in bilateral mid and lower zones of the lungs. Subsequent computed scan of the thorax identified scattered peripheral ground-glass pulmonary opacities congruent with COVID-19 pneumonia. She was started on an initial 5-day course of remdesivir followed by another 10 days of remdesivir due to suspicion for recrudescent COVID-19 infection as evidenced by the persistent polymerase chain reaction positivity for SARS-CoV-2 for more than a month (Table). This was further supported with evidence of viable SARS-CoV-2 in viral cultures (Table). Serology demonstrated evidence of COVID-19 infection but insufficient serological response despite recovering from native disease (Table).

In view of the patient’s prolonged infection, Pfizer-BioNTech mRNA COVID-19 vaccination was administered to boost the immune response and assist in the virological clearance of the SARS-CoV-2 viral infection (Table). Two days following vaccination, SARS-CoV-2 was undetectable based on cycle threshold cutoff value of 40 and remained persistently negative thereafter. Unfortunately, the patient had morphological relapse after clearance of SARS-CoV-2. The patient was offered azacytidine and venetoclax chemotherapy for her relapsed disease. Serology postvaccination showed good immunological response to the mRNA COVID-19 vaccination despite ongoing chemotherapy (Table).

Scant literature suggests acute myeloid leukemia patients with COVID-19 can have their therapy adjusted to avoid intensive chemotherapy.1 Other centers have proceeded with intensive chemotherapy after obtaining a SARS-CoV-2 undetectable on polymerase chain reaction.2 For her, in view of persistent cytopenia, fever, and radiological findings, the chemotherapy was postponed until virological clearance. During her vaccination the patient was monitored inpatient for severe immune reactions such as anaphylactic reactions, thrombocytopenia, myocarditis/pericarditis, or antibody-dependent enhancement side effects, which did not occur.3 This may partly be due to her severe immunocompromised status. Interestingly, she achieved a good serological response 28 days after first vaccination dose. This might be due to either vaccination triggered immune response or a delayed response to her prior COVID-19 infection.

Data is limited for acute myeloid leukemia with COVID-19, and to our knowledge, this is the first case report of a Pfizer-BioNTech mRNA COVID-19 vaccination given during an active COVID-19 infection in an immunocompromised patient to clear the infection. In conclusion, this case highlights the difficulties of treating hematological malignancies in the current pandemic. More vaccination studies...
should be conducted on immunocompromised patients who have active or recovered from COVID-19 infection to better understand the durability of the immune response toward native COVID-19 infection, COVID-19 vaccination, or a hybrid of both.

### Table: Summary and Sequence of Coronavirus Investigations

| Days       | Cycle Threshold Values (cycles) | Serology C Pass (%) | Serology Roche N (U/mL) | Roche S (U/mL) | SARS-CoV-2 Culture | Respiratory Multiplex | Key Events                                      |
|------------|--------------------------------|---------------------|-------------------------|----------------|-------------------|-----------------------|------------------------------------------------|
| 04/23/2021 |                                |                     |                         |                |                   |                       | Coronavir s 229E detected                            |
| 04/29/2021 | 16.22                          |                     |                         |                |                   |                       | Start of first cycle of 5 days of Remdesivir           |
| 05/02/2021 | 14.6                           |                     |                         |                |                   |                       | End of first cycle of 5 days of Remdesivir            |
| 05/03/2021 |                                | 0                   |                         | 1.18           |                   |                       | Positive for viable and infective virus                 |
| 05/11/2021 | 16.3                           |                     |                         |                |                   |                       | Start of second cycle of 10 days of Remdesivir       |
| 05/12/2021 | 21.6                           | 0                   |                         | 1.09           |                   |                       | Coronavirus 229E not detected                         |
| 05/16/2021 | 22.7                           |                     |                         |                |                   |                       | End of second cycle of 10 days of Remdesivir          |
| 05/19/2021 | 26.5                           |                     |                         |                |                   |                       | First Pfizer-BioNTech vaccination                     |
| 05/21/2021 |                                |                     |                         |                |                   |                       | First Negative PCR nasopharyngeal swab                |
| 05/25/2021 | 38.3                           |                     |                         |                |                   |                       | Second Pfizer-BioNTech vaccination                    |
| 05/27/2021 | 30.2                           |                     |                         |                |                   |                       |                                                      |
| 05/30/2021 | 35.1                           |                     |                         |                |                   |                       |                                                      |
| 06/02/2021 | 38.8                           |                     |                         |                |                   |                       |                                                      |
| 06/04/2021 |                                | 20.97               | 8.2                     | 0.593          |                   |                       |                                                      |
| 06/07/2021 | 34.9                           |                     |                         |                |                   |                       |                                                      |
| 06/09/2021 |                                |                     |                         |                |                   |                       |                                                      |
| 06/11/2021 | PCR undetectable               |                     |                         |                |                   |                       |                                                      |
| 06/12/2021 | PCR undetectable               |                     |                         |                |                   |                       |                                                      |
| 06/30/2021 |                                |                     |                         |                |                   |                       |                                                      |
| 07/01/2021 | PCR undetectable               | 94.465              | 29.08                   | 175.9          |                   |                       |                                                      |
| 07/07/2021 | PCR undetectable               | 98.845              | 29.6                    | 894.5          |                   |                       |                                                      |

PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Cycle threshold values refer to the number of PCR cycles required for viral RNA to be amplified to reach a detectable level.
Serology C pass, refers to the percentage of neutralizing antibodies toward the receptor binding domain of the SARS-CoV-2 virus spike protein.
Serology Roche N refers to the titers of antibodies specific to the nucleocapsid core protein for the SARS-CoV-2 virus.
Roche S refers to the titers of antibodies specific to the SARS-CoV-2 virus spike protein.
SARS-CoV-2 culture refers to the viral culture of the SARS-CoV-2 virus that demonstrates viable virions capable of infecting human cells.

References

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