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CASE REPORT

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Janus-faced course of COVID-19 infection in patients with hematological malignancies

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The COVID-19 pandemic affects most countries of the world resulting in significant morbidity and mortality from this infection with SARS-CoV-2.[1] It was reported that among others specifically patients with cancer (including patients with hematological malignancies) are at a higher risk of severe and fatal infection.[2] Here, we report three consecutive patients with underlying hematologic malignancies and comorbidities who were admitted to the infectious disease ward at our department because of SARS-CoV-2 infection.

Patient 1 reported weakness and weight loss already for several months, and in his history, he underwent surgery for colonic cancer followed by chemotherapy 23 years ago. He also suffered from diabetes, hypertension, obesity (BMI 26.8 kg/m^2), and coronary heart disease, four additional risk factors for severe SARS-CoV-2 infection.[3] Five days prior to diagnosis of the infection, the patient developed fever and dyspnea. On admission, he had a temperature of 38.5°C, cough, and reported extreme weakness. Though not sensing dyspnea, his blood oxygenation was reduced with peripheral oxygen saturation of 86% and a pO_2 of 58 mm Hg. Leukocyte and lymphocyte counts were reduced, but in addition the differential blood counts revealed 30% of blasts, which were suggestive for acute myeloid leukemia (AML). Bone marrow aspiration confirmed the diagnosis of AML NOS according to the WHO with a DNMT3A mutation. Continuous oxygen supplementation (6 L/min) was necessary to maintain a peripheral oxygen saturation >90% and alertness of the patient. Accordingly, crackling breath sounds were present over both sides of the lung which was in accordance with the finding of infiltrations in the chest X-ray. Under continuous inhalation with physiologic salt solution and oxygen supply, physiotherapy, and medication with hydroxychloroquine, azithromycin, and low-dose prednisone from days 9 to 14, the patient slowly but gradually improved over a period of 1 week with stepwise reduction in oxygen needs to 2 L/min after 10 days. Oropharyngeal swabs taken on days 9 and 12 revealed SARS-CoV-2 clearance with negative PCR results, and the patient could be discharged after 14 days of hospital stay. Based on his age and the comorbidities, palliative treatment with 5-azacytidine was recently initiated.

Patient 2 was admitted with PCR-confirmed SARS-CoV-2 infection and suspected pneumonia. He reported dry cough and increasing weakness but no fever over the preceding 2 weeks. The patient was on current therapy with the known lymphodepleting therapy consisting of four cycles of bendamustine and rituximab until September 2019, followed by three cycles of rituximab maintenance therapy for follicular B-cell lymphoma (FLIPI Score 1) diagnosed 6 years ago. Four years ago, he underwent surgery for renal cell cancer without subsequent radio- and chemotherapy. Additional risk factors were hypertension and obesity (BMI: 31.9 kg/m^2). On admission, the patient reported fever for 2 days, and he had 37.9°C temperature, leukopenia, and reduced oxygen saturation of 90% and a pO_2 of 55 mm Hg. This was paralleled by dyspnea, and bilateral pneumonia was confirmed by CT. With inhalation therapy and combined oral favipiravir and prednisone from days 9 to 13, the oxygen need could be continuously reduced from 8 to 1 L/min until

day 10. Viral clearance was confirmed by two negative PCR tests for SARS-CoV-2 from nasal swabs and complete resolution of respiratory symptoms of the patient, and the patient could be discharged thereafter as cured from COVID-19 13 days after admission.

Patient 3 had a history of hairy cell leukemia diagnosed 10 years ago. Two months ago, 1% hairy cells were detected in the peripheral blood and thus a relapse was suspected. Ten days before admission, the patient developed symptoms with coughing, fever, diarrhea, and loss of appetite. Three days later, SARS-CoV-2 RNA was tested positive in the swab. The patient´s condition worsened during the following week, and he was therefore transferred to our department. Upon admission, the temperature was 37.3°C; he had a leukopenia and tachypnea; and viral pneumonia was confirmed by chest X-ray. The oxygen saturation at ambient air was initially between 87% and with 6 L/min oxygen supply and it increased to 91%, and the patient was admitted to the ICU. Because of the critical situation and the increased signs of inflammation (Table 1), therapy with favipiravir and a beta lactam antibiotic because of bacterial superinfection without isolation of a specific pathogen was initiated. The patient required invasive mechanical ventilation for 13 days and intermediate corticosteroid therapy for 5 days. Thereafter, he was retransferred to our ward, where he still needed supplemental oxygen followed by a stepwise improvement over the next days. After two negative nasopharyngeal swab PCR results, the patient was transferred as free of infection to a rehabilitation center.

Given the limitation of conclusions that can be drawn from the observations in three patients with newly diagnosed or pre-existing hematological malignancies, it appears that those patients may be more susceptible to SARS-CoV-2 infection and subsequent development of severe infection-associated pathologies including pneumonia with poor blood oxygenation. However, pneumonia could be controlled and cured in all patients and none of them died although one patient required intermittent mechanical ventilation and intensive care management because of bacterial superinfection. This observation suggests that hyperinflammation-associated organ failure may be less pronounced in hematological malignancies due to pre-existing (including disease-associated immunosuppression by co-existing newly diagnosed AML in patient 1 and hairy cell leukemia in patient 3) or treatment-related immunosuppression (lymphodepletion induced by bendamustine/rituximab in patient 2). This would be in a line with observations made in other studies where patients with immune deficiency or after solid organ transplantation presented with an uneventful or mild course of SARS-CoV-2 infection.[3-5] However, other studies in patients with chronic myeloid leukemia reported a high susceptibility and severe course of COVID-19 infection along with a high prevalence of bacterial superinfections.[6,7] Adverse outcomes with a fatality rate between 25-55% have also been described in patients with different types cancer, however, the relative mortality was lowest in subjects with haematological malignancies.[8] Along this line, a recent report presented the favorable outcome of COVID-19 infection in an infant with acute myeloid leukemia.[9] Thus, the nature of

TABLE 1 Patients' characteristics and laboratory findings upon admission (reference values in brackets; d1, laboratory parameter on day of hospital admission, d7-d10, follow-up laboratory parameters between day 7 and day 10 of admission)

	Patient 1	Patient 2	Patient 3
Symptoms	Fever, cough	Fever, cough, dyspnea	Fever, cough, dyspnea, diarrhea
Age (y), gender	78, male	63, male	54, male
Additional risk factors	Hypertension, diabetes, coronary artery disease, obesity (BMI: 26.8 kg/m^2)	Hypertension, obesity (BMI: 31.9 kg/m^2)	Hyperuricemia, obesity (BMI: 26.9 kg/m^2)
Leukocyte count G/L (4-10)	1.4	2.4	3.4
Lymphocyte count G/L (1-3)	0.63	0.47	0.17
Hemoglobin g/L (120-160 for women, 130-170 for men)	106	117	118
Platelet count G/L (150-380)	128	121	277
CRP mg/dL (<0.5) d1/d7-d10	43.6/7.42	8.66/0.97	22.7/19.9
IL-6 ng/L (<7) d1/d7-d10	197.7/7.2	99.7/3.6	393.9/28.1
Peripheral oxygen saturation d1	86%	90%	87%
Duration of supplementary oxygen treatment (d)	14	11	24
Duration of fever (d)	12	9	10
Duration of hospital stay (d)	14	13	29
COVID-19 infection outcome	Cured	Cured	Cured
Time from SARS-CoV-2 detection until negativity (d)	14 d	21 d	29 d

Abbreviations: BMI, body mass index; CRP, C-reactive protein; IL-6, interleukin-6.

the underlying malignant disease, anticancer treatment, and immune status along with comorbidities are likely decisive for the course and outcome of COVID-19 infection. In summary, we describe three cases of patients with hematological malignancies indicating that COVID-19 has a Janus-faced presentation in that patient group. While those patients may have increased susceptibility to viral infection and bacterial superinfection, they may not typically develop COVID-19–associated hyperinflammation in the later course of the disease.

CONFLICT OF INTEREST

None of the authors have a conflict of interest in association with that study.

AUTHOR CONTRIBUTIONS

All listed authors contributed to the content of this study.

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