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CLINICAL VIGNETTE

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Management of febrile neutropenia in a breast cancer patient with SARS-CoV-2 infection during dose-dense adjuvant chemotherapy

Key words: febrile neutropenia, SARS-CoV-2, breast cancer, chemotherapy

A 54-year-old woman with clinical stage IIA (pT1c, pN1a, L/V1) invasive poorly differentiated luminal HER2-positive breast cancer [immunohistochemical expression of estrogen receptors 90%, progesterone receptors 50%, Ki67 30%, epidermal growth factor receptor type 2 (3+)] was admitted to the Oncology Department in December 2021 with fever, throat soreness, and pain during swallowing. Symptoms appeared one week after the fourth cycle of dose-dense adjuvant chemotherapy (doxorubicin and cyclophosphamide) with primary granulocyte colony-stimulating factor (G-CSF) support. In March and May 2021, she had received two doses of the mRNA COVID-19 vaccine (Moderna, Spikevax). On admission, she was in fair general condition: Eastern Cooperative Oncology Group Performance Scale grade 1, without dyspnea, oxygen saturation 95% (breathing room air), and the fungal lesions in the oral cavity grade 3 (G3). Common Terminology Criteria for Adverse Events (CTCAE) and Hand-Foot Syndrome G2 CTCAE were observed. The blood test showed leukopenia (G4), agranulocytosis (G4), thrombocytopenia (G2), and an increased level of C-reactive protein (Tab. 1). A polymerase chain reaction analysis (RT-PCR; KIT LabSystem) was performed for SARS-CoV-2 and was positive for the virus core gene (ORF1ab), capsular gene (E), and nucleocapsid gene (N). The blood and urine culture tests were negative. The risk of complications of febrile neutropenia (FN) was assessed at 26 points in the Multinational Association for Supportive Care in Cancer (MASCC) Risk Index [burden of illness as determined by the attending physician at presentation: mild + 5; hypotension systolic blood pressure < 90 mmHg: no + 5; active chronic obstructive pulmonary disease: no + 4; type of cancer: solid tumor + 4; dehydration: + 3; status at the onset of fever: outpatient + 3; age (years): < 60 + 2]. She was admitted to the isolation ward despite being in the low-risk group for poor FN outcome due to clinically significant infection (SARS-CoV-2) and mucosal inflammation G3 (according to the National Comprehensive Cancer Network recommendations). The empiric broad-spectrum antibiotics (ceftriaxone, ciprofloxacin), antifungal drug (fluconazole), G-CSF (filgrastim), intravenous fluids, and probiotics were administered. Due to symptomatic anemia (hemoglobin 7 g/dL), two units of packed red blood cells were transfused. Low-molecular-weight heparin was not considered because of thrombocytopenia (Tab. 1). A chest non-enhanced CT scan was performed in compliance with standard operating procedure (SOP)

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Table 1. Results of laboratory tests performed on days 1, 2, 5, and 8 of hospitalization

	Reference range	1. day	2. day	5. day	8. day
Leukocytes (× 10^9/L)	4.0–10.0	0.09	0.20	2.72	13.09
Neutrophils (× 10^3/μL)	1.9–8.0	0.02	0.11	2.36	11.96
Hemoglobin (g/dL)	11.0–18.0	9.0	7.0	9.2	9.9
Thrombocytes (× 10^9/L)	150–400	54	24	40	68
C-reactive protein (mg/dL)	0.0–0.8	10.4	9.4	5.8	2.7

management in patients with SARS-CoV-2 accepted in December 2021. A moderate level of infiltrate predominantly peripheral in distribution was observed on the chest scan (Fig. 1). On the second day of hospitalization remdesivir was administered with a loading dose of 200 mg intravenously and the next maintenance dose of 100 mg daily for 5 days in total. Therapy was well tolerated with no side effects. After 8 days, the patient in good general condition, with normalization of hematological values and resolution of mucosal inflammation, but with a positive SARS-CoV-2 test, was discharged from the hospital for further isolation at home. After two weeks after the end of hospitalization and after obtaining a negative RT-PCR SARS-CoV-2 test, adjuvant chemotherapy was resumed. The first cycle of paclitaxel 80 mg/m^2 and trastuzumab 8mg/kg was administered. Adjuvant therapy was continued and completed without any other complications.

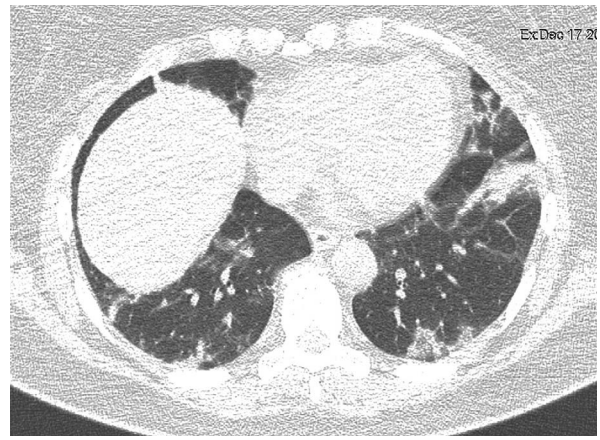

Figure 1. Computed tomography scan of the patient on admission. A moderate infiltrate was observed

Data on febrile neutropenia (FN) management in patients with solid tumors and SARS-CoV-2 infection is limited [1]. Typical treatments of FN are based on empiric or targeted antibiotics, with antifungal drugs (as indicated) and supportive care with strict surveillance of the patient [2]. G-CSF administration in all patients with FN is controversial and applies to specific situations covered by the guidelines [2]. In patients with COVID-19 disease, G-CSF administration may lead to respiratory failure. However, according to European Society for Medical Oncology recommendations, benefits of using G-CSF exceed potential risks [3, 4]. Current data suggest that remdesivir in patients with COVID-19 disease shortens hospitalization and accelerates clinical improvement [5]. In accordance with the Agency for Health Technology Assessment and Tariff System recommendations (3.0 version 28.02.2022), remdesivir therapy should be considered in the high-risk group in the case of a severe course of COVID-19 during virus replication, i.e. sooner than 5 days from the first symptoms of illness, with pneumonia confirmed by medical imaging and oxygen saturation (SpO_2) ≤ 94% (breathing room air). The high-risk group with a severe course of COVID-19 includes also patients with active cancer and immunosuppression (regardless of vaccination status), unvaccinated people, people with suspected insufficient response to vaccination, as well as people with a time from the last dose of the primary series of vaccinations > 6 months [6]. It should be emphasized that this guideline applies to infection with earlier SARS-CoV-2 variants of concern (VC). There is not enough data for reliable recommendations for infection with new SARS-CoV-2 VCs *inter alia* Omikron. Further observations are needed to definitively assess the optimal treatment of patients with FN and SARS-CoV-2 infection.

Conflict of interest

Authors declare no conflict of interest.

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