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Impact of persistent coronavirus infection on the treatment of an immunocompromised oncological patient

Abstract

The emergence of the coronavirus pandemic in 2020 has challenged many aspects of the management of clinical care. It has negatively impacted the already overwhelmed healthcare system in Poland, leading to further limitation of access to specialist care, delay of treatment and even failure to initiate it. Patients with severe, rapidly progressing diseases such as cancer, are among those most adversely affected. Immunocompromised patients are prone to persistent COVID-19 infection and re-test positively even when asymptomatic. In this case report, the authors present an immunocompromised patient with follicular lymphoma and active tuberculosis, who re-tested positive for SARS-CoV-2 in real-time polymerase chain reaction and rapid antigen tests twenty-two times over seventeen weeks of hospitalisation in the isolation ward in University Clinical Centre in Gdansk, Poland. The management of her oncological treatment was significantly disturbed by prolonged isolation and organisational issues arising from the coronavirus pandemic.

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Key words: COVID-19 pandemic, SARS-CoV-2 infection, immunocompromised host, follicular lymphoma, persistent infection, critical illness

Abbreviations

ARDS — acute respiratory distress syndrome
RT-PCR — real-time polymerase chain reaction test
ER — emergency department
UCC — University Clinical Centre

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R-CHOP — chemotherapy based on a combination of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone
FL — follicular lymphoma
TB — tuberculosis
R-MIV-AT — chemotherapy based on a combination of rituximab with high-dose methotrexate, ifosfamide and vincristine

Introduction

Coronavirus disease 2019 (COVID-19), an acute respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first detected and identified in November 2019 in Wuhan, Hubei, China, initiating the worldwide pandemic [1]. The first case of COVID-19 in Poland was confirmed on March 4th, 2020. Up until November 2021, over 3 million cases were identified in Poland, leading to over 75 000 deaths [2]. Symptoms vary from none or mild to severe, including acute respiratory distress syndrome (ARDS). Among the most vulnerable individuals are those primarily or secondarily immunocompromised, such as the elderly, patients with multiple comorbidities, and cancer [3].

Oncological patients require meticulously planned, uninterrupted courses of treatment and often constant palliative care. With the frequent reassignments of healthcare professionals to facilities or wards dedicated to COVID-19 patients, the pandemic poses a challenge to healthcare providers to maintain adequate and continuous oncological and palliative care. In oncological patients with active COVID-19 infection, the course of oncological treatment may be interrupted or halted until the patient's viral RNA is eliminated, proven by a negative real-time polymerase chain reaction test (RT-PCR) or rapid antigen test [4]. However, in immunocompromised individuals who do not produce immunoglobulin antibodies against SARS-CoV-2, an infection can turn into the persistent presence of viral RNA, with repeatedly positive tests for weeks or months [5]. In this report, the authors present the case of an immunocompromised patient with disseminated follicular lymphoma, active pulmonary tuberculosis, and COVID-19 infection that persisted for 17 weeks of hospitalisation.

Case report

A 48-year-old female patient was admitted to the Emergency Department (ED) at University Clinical Centre (UCC), in December 2020 presenting with progressive paresis of lower limbs. Earlier that year she had undergone a full R-CHOP regimen (based on a combination of rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone), radiation therapy to the central nervous system (CNS), and three cycles of maintenance therapy for advanced follicular lymphoma (FL) with bone marrow and CNS involvement (grade 3B stage IV). Additionally, she had a medical history of active pulmonary tuberculosis (TB), neurologic urinary and faecal incontinence, vincristine-induced peripheral neuropathy and Sjögren's syndrome. A month before admittance to the ED at the UCC, she had been briefly hospitalised in a different hospital due to a COVID-19 infection confirmed with (RT-PCR) and discharged with no symptoms of respiratory tract infection. Upon admission to the UCC patient presented with a mild fever hence, as per hospital policy, an RT-PCR test for SARS-CoV-2 was conducted, and the patient again tested positive for COVID–19. Subsequently, she was transferred to the isolation ward for COVID-19 patients, where she was put in an additional isolation room due to active TB.

Due to signs of progression of the underlying condition, palliative radiation therapy to the spinal cord was recommended by a consulting oncologist, provided she tested negative for SARS-CoV-2. In the meanwhile, the hospital policy allowed for the intra-hospital transfer of patients provided they tested negative in Abbot antigen rapid tests. The patient had tested positive in RT-PCR four times in the subsequent three weeks, eventually, on the day 23rd of hospitalisation, she tested negative in a rapid antigen test. In the following days, she underwent radiation therapy to CNS and one cycle of immunochemotherapy R-MIV-AT (combination of rituximab with high-dose methotrexate, ifosfamide and vincristine) in the Clinic of Oncology and Radiotherapy and the Clinic of Haematology and Transplantology in the UCC, respectively. The second transfer to the isolation ward was made directly from the Clinic of Haematology and Transplantology in the UCC, where the patient had presented with fever, pharyngitis and pulmonary crackles. The patient underwent bronchoscopy, and bronchoalveolar fluid was analysed with multiplex RT-PCR that detected SARS-CoV-2 RNA. The diagnosis of re-infection of COVID-19 was thus established again.

In the following weeks of hospitalisation in the isolation ward, the therapeutic team had numerous clinical teleconsultations with the haematology specialists to establish further courses of chemotherapy. Eventually, the patient received another cycle of R-MIV-AT immunotherapy as per instructions from consultants. The chemotherapy was administered by the isolation ward therapeutic team.

After 7 weeks the patient was discharged home from the isolation ward with instructions to continue chemotherapy treatment as planned in the Clinic of Haematology in the UCC. In April 2021, seven days after the discharge, she tested positive in an antigen rapid test twice upon re-admission. Hence, per hospital policy, she could not be admitted to the Clinic and was instead admitted to the isolation ward once more, solely to receive chemotherapy. The patient had to spend another 7 weeks in the isolation ward where she continued the 3rd and 4th cycles of R-MIV-AT.

In April 2021, in a follow-up MRI scan of CNS, a partial remission of FL was identified. According to the consulting haematology specialist, there were indications to administer the final cycle of R-MIV-AT and eventually continue to the consolidation therapy. However, due to the considerable reduction of COVID-19 cases in Poland, in May 2021 the decision was made to shut down the isolation ward. Hospital policy did not allow for the patient to be transferred to the Clinic of Haematology in UCC, and other facilities in Poland presented a similar approach to patients with persistent positive re-tests. Until the very last day in the isolation ward, the patient was being tested for SARS-CoV-2 both with RT-PCR and rapid tests. Each time she re-tested positive. Eventually, on May 23rd, 2021 — the final day of the ward's functioning, The patient was transferred to the Institute of Haematology in Warsaw to continue treatment. In June 2021, due to acute respiratory distress and multiple organ dysfunction, she died.

Discussion

The emergence of the COVID-19 pandemic had generated unforeseen issues with the management of oncological patients. With an already overwhelmed healthcare system in Poland, the pandemic restrictions made diagnostics and the onset of oncological treatment even more problematic. Telemedicine had significantly advanced, however, in some cases physical examination of the patients may be delayed or non-existent, leading to misdiagnosis. Active coronavirus disease in immunocompromised patients delayed diagnostics and treatment, as physicians often decided to temporarily halt or postpone aggressive oncological treatment [4]. The present case demonstrates an example of such complications.

For the presented patient, hospitalisation in the isolation ward significantly hindered the efficiency of her oncological treatment. At every step of the therapeutic path, the COVID-19 therapeutic team met obstacles — each procedure or pre-planned transfer required numerous virological tests that persistently showed the presence of viral RNA. Her hospitalisation overlapped with the peak of the COVID-19 pandemic in Poland when the strictest restrictions regarding the performance of clinical procedures were established by the government and within the hospitals.

For the present immunocompromised patient, numerous mandatory nasopharyngeal swabs for SARS-CoV-2 were persistently positive. During a total of 17 weeks of isolation, the patient had been tested 22 times for SARS-CoV-2 (n = 8 RT-PCR and n = 14 rapid tests) to transfer her to a facility specialising in haematology. In March and May of 2020, serology tests showed that the patient did not produce immunoglobulin antibodies against SARS-CoV-2. Consulting infectious diseases specialist assessed the patient as actively contagious. While on the isolation ward, the patient did not show signs of upper respiratory tract infection other than fever, nor did she require oxygen therapy, convalescent plasma, and antiviral agents. Due to hospital policy and scarcity of medication at the time, she was not eligible for remdesivir treatment.

In this case, the patient's therapeutic process was complex due to her comorbidity, hence she required various clinical consultations. Most of them were conducted remotely via telephone with a rotating clinician. Each therapeutic decision took up more time compared to the rest of the isolated patients. Due to the rotation of staff, the COVID-19 team relied fully on consulting specialists in terms of administering chemotherapy as well as managing its complications, such as pancytopenia and neutropenic fever. Due to resulting interruptions, the management of care was periodically not sufficient.

At the same time, prolonged isolation and organisational issues due to the never-ending positive re-tests loop resulted in the deterioration of the patient's mental health, who was eventually diagnosed with depression and anxiety. She required regular psychological counselling and psychiatric consultations. Other aspects of the widespread morbidity in times of pandemic are prolonged hospitalisations, often in isolation; and the necessity to cope with stress, worry and fear — alone. The proactive approach to mental health plays an important role in the process of convalescence, as depression and anxiety disorders may impair recovery [6].

Upon the final decision to shut down the isolation ward, significant organisational issues arose concerning the transfer of the patient, who still required care and had indications to continue chemotherapy. The conditions for admittance to the hospital had not yet changed, and the team committed two full workdays entirely in search of an institution in Poland that would

admit a haematological patient with a positive SARS-CoV-2 test. When the Institute of Haematology and Transfusion Medicine in Warsaw eventually accepted the patient, an emergency COVID transport needed to be arranged.

Our case demonstrates — on the example of an individual patient — to what extent the coronavirus pandemic affected not only the management of specialistic care but also the management of hospitals. Despite the existence of efficacious cancer treatment, accessibility can be limited by direct and indirect factors caused, or revealed, by the pandemic.

Declaration of conflict of interests

All authors declare that they have no conflicts of interest.

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