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Case report

Chemotherapy resumption in ovarian cancer patient diagnosed with COVID-19

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1. Background

COVID-19 pandemic has imposed a great challenge in the management of patients with chronic illnesses and more specifically cancer. Treatment plan of patients with cancer has been modified due to the necessary reallocation of healthcare resources in order to cope with the pandemic (Ramirez, 2020) and the risk of increased morbidity and mortality among cancer patients infected by SARS-CoV-2 (Liang, 2020). Taken into account these issues, most national and international oncological societies have issued guidelines that assist management of cancer patients throughout this crisis (Burki, 2020).

However, the disease evolves rapidly, and there is continuous need for reliable clinical information. This would allow us to address the following issues in cancer patients: a. the preventive measures that should be implemented to decrease the likelihood of infection, b. the recognition of risk factors that impose the greater threat from COVID-19 and c. the outcome and further management of cancer patients infected by the SARS-CoV-2.

We present the case of an ovarian cancer patient who successfully resumed her chemotherapy immediately after the diagnosis and hospitalization for COVID-19 pneumonia.

2. Case study

A 60-year old woman with a history of recurrent ovarian cancer presented in the emergency department on March 28th due to fever up to 38.5 °C and pain in the right chest. Symptoms had developed hours prior her admission.

The patient was initially diagnosed 20 months ago with stage IIIc high grade serous ovarian cancer and was treated with primary debulking surgery and frontline treatment with Paclitaxel, Carboplatin and Bevacizumab. The patient experienced disease recurrence. The most recent recurrence was three months ago. The patient presented with bowel obstruction and pleural effusion requiring hospitalization and chest tube insertion with pleurodesis. She was started on weekly paclitaxel due to platinum refractory disease with symptomatic relief. Last dose of chemotherapy was two days prior to hospital admission. Her medical history also included paroxysmal atrial fibrillation under treatment with carvedilol and enoxaparin. She was a non-smoker and infrequently drank alcohol.

On examination the patient was alert and fully oriented. The temperature was 38.2 °C, the blood pressure was 95/50 mmHg, the pulse 120 beats per minute and oxygen saturation 92%, while she was breathing on ambient air. At pulmonary auscultation there were diminished breath sounds in the right lower lung lobe. The electrocardiogram indicated atrial fibrillation and the chest X-Ray showed blunting of the right costophrenic angle and a small encapsulated pleural effusion (Fig. 1). Laboratory values were unremarkable apart from demarcated leukocytosis with neutrophilia (WBC 27,900/mm^3 neutrophils 96.5%), increased LDH 598U/L as well as C-Reactive protein (CRP) 241 mg/dl and procalcitonin 3.3 ng/ml. Following national guidance during COVID-19 pandemic, the patient was tested for SARS-Cov-2 and the PCR was positive.

The patient was then transferred to a COVID reference clinic for further treatment. She was treated with a combined regimen of piperacillin-tazobactam, hydroxychloroquine and azithromycin. A CT scan was performed without typical evidence of pneumonia. Blood and urine cultures were negative and fever resolved at day 3 of hospitalization. The patient experienced diarrhea on days 6 and 7. Stool exams were negative for fecal leukocytes and C. Difficile by enzyme immunoassay for toxins A and B. Diarrhea was attributed to COVID-19 and resolved automatically. Two subsequent PCR tests for SARS-CoV-2, performed 24 h apart were negative and the patient was discharged after 12 days of hospitalization.

Two weeks post discharge the patient returned to our clinic for evaluation. The patient was afebrile since her discharge and she only complained for abdominal discomfort. Physical examination and laboratory values were unremarkable and her discomfort was attributed to the recurrent ovarian cancer. At that time point, the patient fulfilled all the criteria to discontinue transmission-based precautions for

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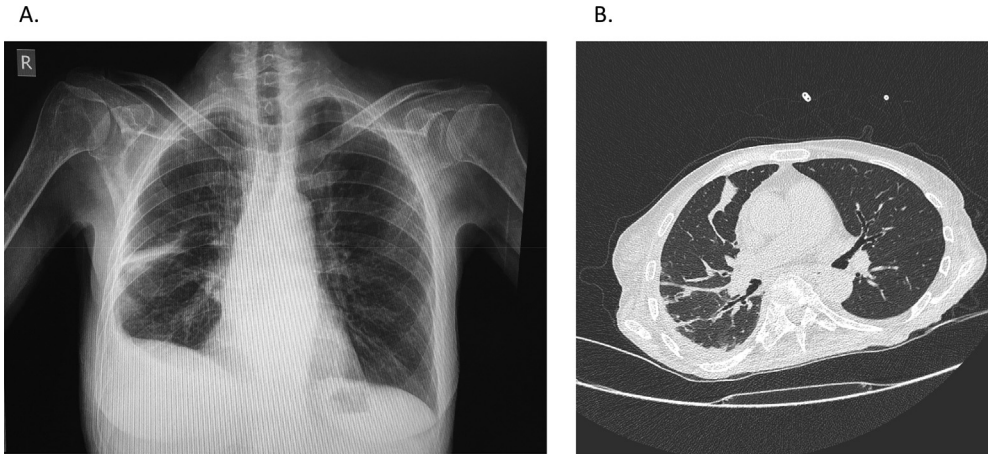

Fig. 1. Chest X-ray(A) and CT scan (B) of the patient at day of hospital admission.

COVID-19 patients, ie. more than two week had passed since initial symptoms and more than three days since full symptomatic recovery. The patient had two negative results in molecular assays for detection of SARS-CoV-2 RNA from consecutive specimens collected at least 24 h apart and she was in need for medical treatment for her symptomatic recurrent ovarian cancer. On the basis of the above factors, chemotherapy resumption was decided. A third PCR test for SARS-CoV-2 was negative and the patient resumed weekly paclitaxel treatment. Currently, she has received three weekly paclitaxel doses without any significant toxicity. A serological test was available and performed to the patient at her second chemotherapy, but the patient was tested negative for IgG and IgA antibodies against SARS-CoV-2.

3. Discussion

To our knowledge this is the first case report of an ovarian cancer patient, which resumed chemotherapy during the convalescent phase of COVID-19 infection without any complications.

Patients with cancer suffer from bacterial and viral infections during their course of treatment (Rolston, 2017). However, these infections do not usually modify their standard care of treatment. In regard to SARS-CoV-2 infection there is limited data about the clinical course of patients with cancer under chemotherapy. Clinical equipoise exists about the optimal time of anticancer treatment resumption. Equally important dilemmas are the role of immunosuppressive chemotherapy in the clinical course of COVID-19, as well as the risk of reinfection.

Currently, there are no instructions regarding the optimal time of cancer treatment re-initiation, as well as the safety of chemotherapy resumption. In the case of SARS-CoV-2, detection of neutralizing antibodies against the virus (seroconversion) signifies recovery and lower risk of re-infection. In a study announced as a preprint in medrxiv (Wu et al., 2020) 94% of 175 patients diagnosed with clinically mild COVID-19, developed neutralizing antibodies within 2 weeks from symptom onset. However, 30% patients failed to develop high titers of neutralizing antibodies, even though their disease duration was similar to the remaining patients. In addition, neutralizing antibodies were undetectable in 6% of patients. Possibly other immune responses may contribute to the recovery of these patients, but it is unclear whether such patients remain at risk for re-infection. In our case, the decision to resume chemotherapy was based on clinical criteria and laboratory tests indicating her recovery from COVID-19. The patient had two negative PCR tests prior to hospital discharge and a third one negative prior to chemotherapy resumption. In addition, she was tested for antibodies against COVID-19 but the test was negative. A recent study in France showed that patients with cancer – especially those that had recently received chemotherapy – had lower detection rate of SARS-CoV-2 antibodies (Solodky et al., 2020).

Our patient had a mild COVID infection, despite her age and comorbidities. It should be also emphasized that COVID 19 infection did not recur, despite the early resumption of chemotherapy. Currently, there are no data on the course of actively treated patients post COVID infection. On the contrary, there are some data with respect to the course of COVID, while receiving treatment. One study from China indicated an increased number of cancer patients actively treated with chemotherapy with COVID-19, who had a dismal prognosis (Liang, 2020). However, studies from United States did not detect increased mortality from COVID-19 among patients with cancer (Miyashita, 2020).

Could immunosuppression caused by cancer per se and the anticancer treatment ameliorate the hyperinflammatory state of COVID? We know that severe and critically ill COVID-19 patients are characterized by a hyper-inflammation response (Giamarellos-Bourboulis, 2020).Based on reports, immunomodulatory agents as tocilizumab, an Interleukin-6 inhibitor a indicate improved clinical outcome in these patients (Xu, et al., 2020). On the other hand, cancer and chemotherapy induce an immunosuppressive state which could counterbalance the hyper inflammatory response associated with severe coronavirus disease and lead to a milder course. Accumulating data from international registries is anticipated to provide further insight for the exact role of cancer and chemotherapy in the clinical outcome of COVID-19.

In summary, this is the first case of an ovarian cancer patient diagnosed with COVID-19 while on chemotherapy whose treatment reinitiated successfully during the convalescent phase of the viral infection. Our case adds to previous series indicating that actively treated cancer patients could have milder course of COVID-19 infection. It also suggests that good performance status and negative PCRs could serve as possible indicators to resume chemotherapy. Further studies will confirm the validity of these findings.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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