

Case Report

3 Cases of Covid 19 Reinfection and Review of Literature

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Abstract

Cancer patients are at higher risk to develop severe COVID-19 forms. SARS-CoV-2 reinfection occurred during the current pandemic period. Thanks to previous studies, we know that the number of patients who need to hospitalization in intensive care units is higher during reinfection.

We describe three cases of SARS-CoV-2 reinfection in cancer patients who developed mild symptoms. We think that the reason for why they did not develop a severe form of COVID-19 is that all of them received at least one dose of approved vaccines.

INTRODUCTION

Tumour growth and anticancer therapy cause a decrease in the efficiency of the immune system. This is why we can consider cancer patients as a major vulnerable group, at risk of poor prognosis, compared with patients without cancer [1]. Particularly, lung cancer patients often have severe forms of COVID-19, due to the fact that SARS-CoV-2 is a virus infecting the respiratory tract, and they have a higher risk of dying than other cancer patients [2].

Basing on a previous study, the most frequent cancer subtype in patients with reinfection is lung cancer. Moreover, SARS-CoV-2 reinfection is associated with an increase of requiring hospitalization in intensive care unit [3].

A review of case reports and case series reported a case of SARS-CoV-2 reinfection in an 80 years old woman, treated with chemotherapy because of a haematological malignancy. She developed mild symptoms during first infection while she had severe symptoms, resulting in death, during the reinfection [4].

CASE PRESENTATIONS

We reported three cases of SARS- CoV- 2 reinfection, 2 in lung cancer and 1 in prostate cancer patients respectively. The 3 cases expressed mild symptoms in both first infection and reinfection.. Patients' characteristics are shown in Table 1.

Case 1

58-age man with lung adenocarcinoma, staging pT3 Nx Mx, G3, PD-L 1 > 50%. DNA mutations and RNA fusions were not found. He stopped smoking in 2021 and he does not have any comorbidity. His familiar anamnesis reveals his father developed cirrhosis, and then degenerated to a liver cancer. He infected

himself with SARS- CoV-2 twice. First infection occurred in January 2021 when the patient did not know he had already a lung cancer. A negative RT- PCR test result was noticed 20 days after. Patient's reported symptoms were fever (38.5° C) and mild cough. Second infection occurred in January 2022. A negative RT-PCR test result was found 19 days after. Again, patient's reported symptoms were fever (39° C) and mild cough. The patient did not require hospitalization, O2 therapy or intensive care unit during neither infection.

A January 2022 CT scan showed ground glass figure described as a result of a recent inflammatory process not yet resolved.

Case 2

63-age man with metastatic lung adenocarcinoma PD-L1<1%. Brain metastases were treated with a pan-encephalic radiotherapy in January 2022. He smokes one cigarettes pack per day and he does not have any comorbidity. His familiar anamnesis reveals his mother developed a gastric cancer. He infected himself with SARS- CoV-2 twice. First infection occurred in September 2020. Patient's cancer diagnosis was done in December 2021, so he did not know he had already a lung cancer in that moment. A negative RT-PCR test result was found 10 days after. Patient's reported symptom was coryza. Second infection occurred in January 2022. A negative RT- PCR test result was found 17 days after. Patient's reported symptoms were coryza and fever. The patient did not require hospitalization, O2 therapy or intensive care unit during neither infection.

Case3

71-age man with non-metastatic castration-resistant prostate cancer. He infected himself with SARS- CoV- 2 twice. First infection occurred in March 2020. A negative RT-PCR test result was found

Table 1: Clinical data of reinfected patients.

PATIENT	1	2	3
AGE (years)	58	63	71
CANCER type	Lung adenocarcinoma PT3 Nx Mx	Metastatic adenocarcinoma (metastases)	lung (brain) Stage IV Non-metastatic Castration-resistant prostate cancer
COMORBIDITY	None	None	- Hypertension - Diabetes - Osteoporosis
SMOKE	No	One pack per day	No
TREATMENT	Carboplatin- Pemetrexed	Carboplatin- Pemetrexed	LHRH agonist
FIRST INFECTION (Time to negativization)	20 days	10 days	14 days
SYMPTOMS during first infection	- Fever (38.5°C) - Mild cough	- Coryza	- Fever (38.7° C) - Dyspnea - Cough
SECOND INFECTION (Time to negativization)	19 days	17 days	9 days
SYMPTOMS during second infection	- Fever (39°C) - Mild cough	- Coryza - Fever	- High fever - Cough
VACCINES before reinfection	- I dose (Comirnaty)	- I dose (Vaxevria)	- 2 doses (Comirnaty)

14 days after. Patient's reported symptoms were fever (38.7°C) for 1 week, dyspnea and cough. He required hospitalization for 3 weeks, intubation and invasive mechanical ventilation in ICU. Second infection occurred in April 2022. A negative RT-PCR test result was found 9 days after. Patient's reported symptoms were high fever and cough. He did not require hospitalization, O2 therapy and ICU.

DISCUSSION

SARS- CoV-2 infection is characterized by different clinical manifestations ranging from asymptomatic to symptomatic. It is important to underline that in elderly and immunocompromised individuals, coronavirus infections may lead to severe pneumonia and subsequently, the death of the patient [5-7].

In the progression of COVID-19, two proteins have an important role: the angiotensin-converting enzyme-2 (ACE2) and C-X-C motif 10 (CXCL10). According to literature findings, ACE2 and CXCL10 are overexpressed in lung cancer. Elevated levels of ACE2 receptor could explain SARS-CoV-2 entry in lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC) [8].

A study showed that ACE2 is differentially expressed in kidney chromophobe (KICH), breast invasive carcinoma (BRCA), prostate adenocarcinoma (PRAD), thyroid carcinoma (THCA), liver hepatocellular carcinoma (LIHC) and stomach adenocarcinoma (STAD) [9]. So we can consider prostatic cancer patients as elevated risk patients for SARS-CoV-2 infection too.

COVID-19 scenario is continuously developing. There are some limitations and potential bias we should discuss. First, new variants emerged during this period of pandemic. Reported Cases were tested for SARS- CoV-2 but sequencing was not done. That is why it is hard to understand which the infectant variant in our patients was. We can just analyse the epidemiological scenario

in the corresponding period of infection and, according to that, hypothesize the most probable infectant variant. Second, ACE2 and CXCL10 were not dosed. For this reason, we can only refer to previous studies and, based on these, we could define the higher risk of developing severe forms of disease in cancer patients we reported about.

Patients we reported about did not develop a severe COVID-19 form during the reinfection even if they can be considered as high risk patients because of the tumour growth and likely because of the ACE2 up regulation. As literature reported, during the reinfection the risk to develop a severe form and to require hospitalization is higher. In fact, a study that involved 1024 patients with solid cancer diagnosis who underwent SARS-CoV-2 reinfection showed that mortality rate of COVID-19 reinfection was 34.3%, and reinfection rate was 3.1% in patients with solid cancer. Moreover, another important data that emerged from the same study is that during reinfection, a higher percentage of patients' needs to receive intensive care support than during the first infection (62.5% vs. 9.5%, p=0.002) [3].

These events did not happen in our patients. A reason for why our lung cancer patients did not develop a severe form of COVID-19 could be the absence of active anticancer therapy during the reinfection period. In fact, we know from literature that anticancer treatment within 14 days before COVID-19 diagnosis is associated with more severe forms of COVID-19 [1].

According to previous studies, ADT does not worsen COVID-19 risk and trajectory. Indeed, ADT as a cancer treatment might be safely administered to patients during the COVID-19 pandemic [10,11]. Prostate cancer patient we reported about received an LHRH agonist and he did not develop a severe form of COVID 19 disease during the second infection, probably due to vaccination received.

Vaccines changed COVID-19 scenario since they started to be inoculated. Indeed, thanks to the vaccines use, mortality has been reduced, as well as the risk to develop severe forms of SARS-CoV-2 related pneumonia. Our patients received at least one dose of the vaccines approved, as shown in Table 1. Therefore, this might explain the reason for the development of mild symptoms during the second infection. According to results published in an ESMO review, vaccination against COVID-19 for cancer patients seems overall safe and immunogenic after well-conducted vaccination schedules, even if the seroconversion rate is lower, lagged or both compared to the general population [12].

To summarize, none of our SARS-CoV-2 reinfected patients developed a severe COVID-19 form. It is hard to understand which is the main reason for that, but we assume a fundamental role of COVID-19 vaccine that all of them received.

It could be interesting and useful to continue to study reinfection in cancer patients so that could be clearer the role of vaccines in the development of different forms of the SARS-CoV-2 associated disease.

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