Cancer recurrence or aggravation following COVID-19 vaccination

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Implication for health policy/practice/research/medical education:
The effectiveness and safety of the COVID-19 vaccine for patients with malignancies are one of the factors that are considered regarding this vaccine.


Introduction
SARS-CoV-2 viral infection leads to an acute respiratory syndrome and consequently COVID-19 global pandemic due to the rapid respiratory spread of the virus.

Millions of people have received numerous COVID-19 vaccine injections to prevent COVID-19 (1). The recurrence or flare-up of several diseases after receiving the vaccine is one of the concerns of COVID-19 vaccination, as well as other vaccines, which include autoimmune disorders, rheumatic diseases, and cancers (2).

Vaccine efficacy, safety, and potential side effects, such as disease recurrence, should be investigated, and are required for these vaccines to be used prior to the administration to certain individuals suffering from autoimmune diseases or cancers.

We are attempting to investigate potential side effects, including cancer recurrence following the COVID-19 vaccination in this narrative review study.

Methods
The desired contents of the published articles were extracted by searching international databases, such as
Efficacy and safety of the COVID-19 vaccine in cancer patients

The COVID-19 pandemic and vaccination have emerged in the last 2-3 years. However, further studies are required on various aspects of the diseases, vaccines, and the potential side effects. The efficacy and safety of COVID-19 vaccines are of great importance in patients with malignancy. Limited studies have been conducted in this regard, which is briefly reviewed.

Togashi et al (3) assessed the anti-SARS-CoV-2 IgG (anti-severe acute respiratory syndrome coronavirus 2 spike immunoglobulin antibody) titer after two doses of BNT162b2 vaccine in 145 individuals, including 57 patients with urothelial cell carcinoma and 28 patients with renal cell carcinoma in the case group and 60 healthy individuals in the control group. Laboratory results showed that 100% of the control group, 96% of patients with renal cell carcinoma, and 90% of patients with urothelial cell carcinoma were seropositive. Their retrospective study showed that the antibody titer is not significantly reduced after two doses of the COVID-19 vaccine in patients who are actively receiving anti-cancer treatment. Moreover, the antibody titer and seropositivity were not significantly different among patients with renal cell carcinoma and urothelial cell carcinoma, since both groups had adequate levels of antibody.

Li et al (4) investigated 738 patients with advanced metastatic genitourinary malignancy, 462 of whom have received the COVID-19 vaccine. They showed 81.8% vaccine protection against infection and 85.7% vaccine effectiveness in preventing hospitalization. The results of their study proved the efficacy and safety of the COVID-19 vaccine and showed that 97.6% of patients with advanced metastatic genitourinary malignancy did not experience severe side effects after vaccine injection.

Paraclinical findings after injection of COVID-19 vaccine in patients with malignancy

Patients with malignancy are concerned about potential lymph node involvement, disease recurrence, and paraclinical findings. In this regard, some studies have been conducted including a case report by Soeder et al (5) who reported a 52-year-old postmenopausal woman with thyroid cancer who developed a firm palpable mass with peripheral erythema in the superior lateral quadrant of the left breast five days after injection of Pfizer COVID-19 vaccine. A new focal asymmetry was reported in the upper outer quadrant of the left breast in the mammography. Five weeks later, magnetic resonance imaging failed to show any suspicious mass or mass enhancement in the upper outer quadrant of the left breast and showed no evidence in favor of auxiliary lymphadenopathy; thus, the patient was informed that the mass has been totally resolved. A retrospective study was conducted to investigate the cortical thickness of lymph nodes in two groups of patients. The first group consisted of 77 patients with benign reactive adenopathy following the mRNA COVID-19 vaccine and the second group consisted of 76 patients with malignant adenopathy due to breast cancer. This study showed that the mean cortical thickness of the two groups was $8.2 \pm 1.5$ mm and $9.8 \pm 5.4$ mm respectively which showed a statistically significant difference between the two groups; however, the lymph node size showed no statistically significant difference between the two groups. The effacement of the hilum of a node was only observed in the malignant nodes (6).

Recently, Andrescian et al (7) reported a 62-year-old man with bone-metastatic prostate cancer with lymph node involvement. The patients received hormone therapy and radiotherapy. No recurrence was observed in the two years of routine follow-up. The latest follow-up in less than three weeks after injection of the second dose of Pfizer COVID-19 vaccine, $^{18}$F-fluorocholine positron emission tomography-computed tomography ($^{18}$F-FCH PET/CT) shows increased F-FCH uptake and enlargement of left auxiliary lymph nodes. Moreover, increased F-FCH uptake in para-aortic, subcarinal, hilar bilateral lymph nodes and para-tracheal have been shown with morphology stability of the lymph nodes compared with the computerized tomography (CT) scan of two years ago. Prostate-specific antigen (PSA) level was not elevated. Moreover, $^{18}$F-FCH PET/CT was repeated 14 weeks later reporting a similar uptake in the mentioned areas reflecting lymphadenopathy as the side effect of COVID-19 vaccination, and not related to the oncology disease.

Considering the importance of lymph node involvement and the risk of malignancy recurrence and the paraclinical alterations in these patients, following the COVID-19 vaccine, and the findings of these studies, further investigations are required in this regard.

Case reports; disease recurrence following COVID-19 vaccine

Panou et al (8) reported two cases of cutaneous T-cell lymphoma in remission for years that had shifted to the reappear phase after receiving the COVID-19 vaccine. The first case was a 60-year-old man with stage T1a/A folliculotrop mucosa fungoides tumor (MF) manifested with multiple patches of alopecia areata manifested on the face, arms, and pubic regions. Over the past two years, the disease has remained at the T1aN0M0 stage with a stable skin patch in the occipital region. Four weeks after the initial vaccine dose, a minor lichenoid induration appeared around the patch. A week later, small nodules appeared. The biopsy confirmed the diagnosis of CD30+ large cell transformation tumor.

The second case involved a 73-year-old woman with
COVID-19 vaccination has led to cancer recurrence in some cases and cancer remission in limited cases. Further studies are required in this regard considering the limited available investigations.

**Authors’ contribution**

Conceptualization: PS and SY.
Validation: PS, SY, LM and RM.
Investigation: PS, SY, SN, LM and RM.
Resources: LM and RM.
Data curation: PS, SY, LM and RM.
Writing—original draft preparation: MM, MSCM, SA, AK, MAEP, MM, PS and SY.
Writing—review and editing: MM, MSCM, SA, AK, MAEP, MM, PS and SY.
Visualization: PS and SY.
Supervision: SN, LM and RM.
Project administration: PS, SY, SN, LM and RM.
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