



Cancer recurrence or aggravation following COVID-19 vaccination

Parisa Soleimani^{1*}, Sepideh Yadollahifarsani^{1*}, Mahsa Motieian², Mahshid Sadat Chenarani Moghadam³, Shahrzad Alimohammadi^{4,5}, Azadeh Khayyat⁶, Mohammad Ali Esmail Pour⁷, Sina Neshat⁸, Narges Alsadat Marashi⁹, Leila Mahmoodnia^{10*}, Rohollah Masomi^{10*}

¹Nickan Research Institute, Isfahan, Iran

²Independent Researcher, Dobbs Ferry, NY, United States

³Department of Dermatology, Radboud University Medical Center, Nijmegen, the Netherlands

⁴Doctoral School of Molecular Medicine, University of Debrecen, Debrecen, Hungary

⁵Department of Immunology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary

⁶Department of Pathology, Resident Physician, Medical College of Wisconsin, Milwaukee, WI, USA

⁷Department of Internal Medicine, Resident Physician, University of NC Health Blue Ridge, Morganton, NC, USA

⁸Department of Pulmonology, Mayo Clinic, Jacksonville 32224 FL, USA

⁹Faculty of Life Sciences, University of Strasbourg, Strasbourg, France

¹⁰Cancer Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

*Parisa Soleimani and Sepideh Yadollahifarsani contributed as the first authors.

ARTICLE INFO

Article Type:
Mini-Review

Article History:

Received: 14 December 2022

Accepted: 25 February 2023

Published online: 15 April 2023

Keywords:

Cancer, Malignancy, COVID-19 vaccine, SARS-CoV-2, Cancer

ABSTRACT

COVID-19 infection has been a global health issue in the past recent years and numerous topics are studied in order to discover its pathophysiology and potential side effects. The potential for disease recurrence following the administration of the COVID-19 vaccine is one of the issues that has recently attracted attention. Several studies have revealed that the COVID-19 vaccines, like other vaccines, may have side effects and, in some cases, they may even deteriorate the underlying illnesses, such as rheumatic diseases, autoimmune diseases, and cancers. The effectiveness and safety of the COVID-19 vaccine for patients with malignancies are one of the factors that are considered regarding this vaccine. Lymph node involvement, disease recurrence, and potential paraclinical changes after receiving the COVID-19 vaccine are some of the concerns of patients with malignancy. In this mini-review, we attempted to investigate cases of cancer recurrence or recovery as well as lymphadenopathy following vaccination.

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.

Please cite this paper as: Soleimani P, Yadollahifarsani S, Motieian M, Chenarani Moghadam MS, Alimohammadi S, Khayyat A, Esmail Pour MA, Neshat S, Marashi NA, Mahmoodnia L, Masomi R. Cancer recurrence or aggravation following COVID-19 vaccination. J Nephroarmacol. 2023;12(2):e10593. DOI: 10.34172/npj.2023.10593.

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

PubMed and Google Scholar between 2020 and 2022. COVID-19 vaccine, SARS-CoV-2, cancer, and malignancy were among the keywords.

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 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 ± 1.5 mm and 9.8 ± 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, Andresciani 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 folliculotropic 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

a 10 years history of early-stage MF (stage T1a/IA) and lymphomatoid papulosis type A (LyP) which was successfully treated by PUVA and was in the remission phase in the past seven years. Ten days after the first dose of the COVID-19 vaccine, skin rashes appeared where LyP was previously observed. Accordingly, LyP type A was confirmed by histology.

It appears that training CD4⁺ and CD8⁺T cells and B cells against SARS-CoV-2 protein antigens is the most common method of production of COVID-19 vaccines. Cancer and COVID-19 produce significant amounts of antibodies leading to T cell exhaustion, as well as COVID-19 vaccination.

Studies have shown that CD30 is expressed on a variety of lymphoid neoplasms, as well as on active B cells and T cells. CD30 is highly expressed in CD4⁺ and CD8⁺ cells and is induced by a variety of antigens in an *in vitro* setting, including mitogens and some viruses. Therefore, relapse can occur as a result of high levels of CD30 expression following the immune system's response to the vaccine antigen and as a result of the overproduction of CD4⁺ and CD8⁺T cells.

Gambichler et al presented a case of primary cutaneous anaplastic large-cell lymphoma (pcALCL) with diffuse lung manifestation (9) which was recovered following COVID-19 vaccination. The prognosis for this rare form of lymphoma is excellent. Despite the high rate of recurrence, 10–42% of patients experience full recovery without treatment. Infection, surgery, and some vaccines are among the factors that have been associated with spontaneous patient recovery.

They presented a 57-year-old man with a 10-year history of recurrent pcALCL with frequent local relapses in the scalp and neck. The last patient's radiotherapy treatments were in February of 2021, following a course of methotrexate, gemcitabine, brentuximab, and radiation therapy.

Ultrasound examination of the cervical region revealed a large pathological lymph node at the end of March 2021. The subsequent computed tomography scan revealed bilateral lung suspicious nodules.

Before restarting lymphoma treatment, the patient noticed the cervical lymph node shrinking and other symptoms disappearing one week after receiving the COVID-19 vaccine. Although not established, it seems that the COVID-19 vaccine has led to disease regression.

Conclusion

The COVID-19 pandemic, its treatment, and its complications are emerging issues and require investigations in various aspects, including the disease recurrence following COVID-19 vaccination. The present study aimed to investigate the cancer recurrence or remission following COVID-19 vaccination as well as lymphadenopathy. It was shown that 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.

Funding acquisition: LM and RM.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323:1239-42. doi: 10.1001/jama.2020.2648.
2. Barbaiya M, Levine JM, Siegel CH, Bykerk VP, Jannat-Khah D, Mandl LA. Adverse events and disease flares after SARS-CoV-2 vaccination in patients with systemic lupus erythematosus. *Clin Rheumatol*. 2022;41:1619-22. doi: 10.1007/s10067-021-05963-6.
3. Togashi K, Hatakeyama S, Yoneyama T, Hamaya T, Narita T, Fujita N, et al. Effect of active anticancer therapy on serologic response to SARS-CoV-2 BNT162b2 vaccine in patients with urothelial and renal cell carcinoma. *Int J Urol*. 2022;29:733-9. doi: 10.1111/iju.14882.
4. Li H, Sahu KK, Kumar SA, Nordblad B, Sayegh N, Tripathi N, et al. A retrospective study to evaluate the efficacy and safety of SARS-CoV-2 vaccine in patients with advanced genitourinary cancers. *Heliyon*. 2022;8:e10583. doi: 10.1016/j.heliyon.2022.e10583.
5. Soeder E, Toro-Pape FW, Lampen-Sachar K. Isolated breast parenchymal changes following COVID-19 vaccine booster. *Radiol Case Rep*. 2022;17:4556-4560. doi: 10.1016/j.radcr.2022.08.094.
6. Hl C, GJ W, Jw L, J S, Lp M, Ht LP. Ultrasound Features to Differentiate COVID-19 Vaccine-Induced Benign

- Adenopathy from Breast Cancer Related Malignant Adenopathy. *Acad Radiol.* 2022;29:1004-12. doi: 10.1016/j.acra.2022.02.015.
7. Andresciani F, Ricci M, Grasso RF, Zobel BB, Quattrocchi CC. COVID-19 vaccination simulating lymph node progression in a patient with prostate cancer. *Radiol Case Rep.* 2022;17:2996-9. doi: 10.1016/j.radcr.2022.05.072.
 8. Panou E, Nikolaou V, Marinos L, Kallambou S, Sidiropoulou P, Gerchristou M, et al. Recurrence of cutaneous T-cell lymphoma post viral vector COVID-19 vaccination. *J Eur Acad Dermatol Venereol.* 2022;36:e91-e93. doi: 10.1111/jdv.17736.
 9. Gambichler T, Boms S, Hessam S, Tischoff I, Tannapfel A, Lüttringhaus T, et al. Primary cutaneous anaplastic large-cell lymphoma with marked spontaneous regression of organ manifestation after SARS-CoV-2 vaccination. *Br J Dermatol.* 2021;185:1259-62. doi: 10.1111/bjd.20630.

Copyright © 2023 The Author(s); Published by Society of Diabetic Nephropathy Prevention. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.