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Vaccines as an Effective Treatment for Triple-Negative Breast Cancer

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Abstract. Breast cancer is a malignant tumor that originates from the breast tissue. Triple-negative breast cancer (TNBC) accounts for a certain proportion of all types of breast cancer, and it is a type of breast cancer that is difficult to treat and highly dangerous. Triple-negative breast cancer (TNBC) lacks three receptors, which leads to its difficulty in treatment. The common treatment methods for triple-negative breast cancer (TNBC) mainly include chemotherapy and immunotherapy. Immunotherapy is a treatment approach that targets the tumor's ability to evade the immune system's attack, helping T cells maintain normal activity and stimulating the immune response. Although chemotherapy leads to a relatively good prognosis, it poses significant harm to the human body. In recent years, there have been many advancements in the use of vaccines for treating triple-negative breast cancer (TNBC). This review article will mainly discuss the current progress, advantages, and challenges of using vaccines to treat triple-negative breast cancer (TNBC).

Keywords: vaccine, triple negative breast cancer, immune response, antibody

1. Introduction

Breast cancer (BC) is a malignant tumor that originates from the breast tissue. It is one of the most common malignant tumors among women worldwide, with its incidence and mortality rates constantly increasing every year [1]. Among them, triple-negative breast cancer (TNBC) is a subtype of breast cancer, which is a highly specific and aggressive malignant tumor, accounting for 10-15% of breast cancer cases. It is defined as lacking the expression of three receptors: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), resulting in poor traditional treatment outcomes and also being the fundamental reason for significant differences with other subtypes of breast cancer [2]. Triple-negative breast cancer has the lowest survival rate among breast cancer subtypes, which is the most challenging to diagnose.) The tumor volume is larger at the time of diagnosis, the proliferation rate is higher, and it is more prone to early metastasis, especially to distant organs such as the lung, liver, and brain. Now, the median survival period has increased from 13.3 months to 18 months[3]. In recent years, there have been many advancements in the treatment of TNBC. Studies have explored targeted therapy and immunotherapy drugs. Currently, the common treatment methods include chemotherapy, immunotherapy, and targeted therapy. Among them, chemotherapy has so far been the main treatment method for early and advanced triple-negative breast cancer.

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Despite these advancements, the treatment of TNBC still faces numerous challenges. The existing phenomena of drug resistance and recurrence in chemotherapy and immunotherapy are widespread, presenting significant challenges for cancer treatment. Another treatment option is tumor vaccines, which are biological agents that stimulate the human immune system to recognize and attack tumor cells. They have dual values of "treatment" and "prevention" in cancer treatment. Tumor vaccines may be effective in preventing breast cancer, activating specific immune responses, generating memory cells that prevent cancer recurrence, and enhancing the immune response against tumor-derived antigens through the amplification of anti-tumor T-cell reactions in the treatment environment. Although there is the treatment option of tumor vaccines, it has not yet become a routine treatment for breast cancer. Therefore, the main purpose of this review article is to explore the effectiveness and safety of vaccines in treating triple-negative breast cancer.

2. Understanding triple-negative breast cancer

Breast cancer cell types encompass Luminal A, Luminal B, HER-2 enriched, basal-like, and normal breast-like subtypes [4].Triple-negative breast cancer (TNBC) refers to a type of breast cancer that lacks the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER-2). Triple-negative breast cancer has the characteristics of high risk and high recurrence rate among all types of breast cancer.This is due to some of its specific features, including gene mutations, abnormal signaling pathways, tumor microenvironment, and other molecular characteristics.The main mutations in triple-negative breast cancer are classified into six types. TP53 accounts for 21.4%, BRCA accounts for 11.6%, BRCA2 accounts for 4.5%, RET accounts for 5.4%, PI3KCA accounts for 2.7%, and PTEN accounts for 3.6% [1]. The high risk is mainly related to the BRCA1 gene mutation. Aberrations in BRCA1 may lead to a deficiency in estrogen receptor expression, and 80% of women with BRCA1 gene mutations suffer from triple-negative breast cancer,with a probability far exceeding that of the general population [5].

Secondly, the Hedgehog signaling pathway comprises three ligands: SHH, IHH, and DHH, with SHH exerting a substantial influence in TNBC. High expression of SHH stimulates the continuous division of TNBC cells and bind to the corresponding receptors on the surface of cancer cells, resulting in their high proliferative capacity and propensity for recurrence,SHH-induced epithelial-mesenchymal transition (EMT) in cancer cells promotes the metastasis of triple-negative breast cancer to distant organs, which is a key reason for the poor prognosis of TNBC patients [4]. Abnormalities in the Notch signaling pathway and abnormalities in Wnt signaling pathway are another critical factor, with FZD6 being one of the receptors highly expressed in TNBC. Activation of the Wnt signaling pathway enhances cellular proliferation and metastatic properties, exacerbating the malignant manifestations of TNBC [6].The cancer stem cells (CSCs) of TNBC are also closely related to tumor recurrence and drug resistance. And the Notch signaling pathway precisely promotes the increase of CSCs. These principal factors collectively contribute to TNBC being the most challenging malignant tumor among various breast cancers to treat.

3. Common treatment methods of triple-negative breast cancer

So far, one of the most common treatment methods for triple-negative breast cancer is immunotherapy. In the tumor microenvironment of TNBC, the expression of TPD-L1 is higher than that in other types of breast cancer. Meanwhile, PD-1 is a transmembrane inhibitory co-receptor expressed on the surface of T cells. When it binds to its ligand, it leads to immunosuppression [7].One of the main reasons for TNBC is the influence of immune escape. In the tumor

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microenvironment, the binding of the PD-1 programmed cell death receptor to the PD-L1 programmed cell death ligand can alter the activity of T cells, causing their death and preventing them from recognizing and attacking the tumor [8]. T cells are a very important type of cell in the immune system, and they have many functions.Firstly, T cells can recognize cancer cells and destroy and kill these cells, thereby inhibiting the growth of tumors. Secondly, the cytokines secreted by T cells will activate other immune cells to enhance the immune response, such as B cells. At the same time, memory T cells can reduce the probability of tumor recurrence.Therefore, the reduced activity of T cells helps tumors evade the attack of the immune system. Immunotherapy is a treatment method developed based on this phenomenon.

Immune checkpoint inhibitors (ICI) can prevent the inhibition of T cells from enabling them to properly recognize and attack tumor cells, thereby enhancing the immune response.However, tumor-infiltrating lymphocytes (TILs) also have an impact on the treatment of immunotherapy, as their presence alters the tumor microenvironment.TILs are monocytes in the tumor microenvironment. The International TILs Working Group has established evaluation criteria based on the presence, density, and distribution of immune cells, dividing them into three categories: high (≥60%), medium (11-59%), and low (0-10%) [9].Studies have shown that patients with TNBC who have a high density of TILs have better responses to ICI treatment and a lower risk of recurrence and death. In general, there are many advantages to treating TNBC with immunotherapy. The treatment effect of immunotherapy is more obvious when the lymphoid infiltration (TIL) and PD-L1 expression levels of TNBC are high, and immunotherapy can also change the tumor microenvironment.

Chemotherapy is another common treatment method. Neoadjuvant chemotherapy (NAC) is administered before surgery and is suitable for patients with early-stage and most locally advanced triple-negative breast cancer (TNBC).NAC not only helps to shrink tumors and increase the resection rate during surgery, but also enables us to understand the sensitivity of tumors to therapeutic drugs [10]. Adjuvant chemotherapy is usually administered after surgery, helping early TNBC patients eliminate tumor cells and prevent recurrence. Anthracyclines and taxanes are two types of chemotherapy drugs used in neoadjuvant and adjuvant treatments.pCR is an important indicator for evaluating the therapeutic effect of NAC. The higher the pCR rate, the better the killing effect of NAC on tumors and the lower the risk of recurrence [11].Some studies have shown that NAC has a higher pCR rate in treating TNBC patients with BRCA1 mutations compared to other TNBC patients, but further research is still needed to confirm this phenomenon [11]. To increase the pCR rate, immunotherapy can also be combined with chemotherapy for the treatment of TNBC.The combined therapy has many advantages. Besides the most important one, which is to increase the pCR rate, the combined therapy can also better reduce the risk of recurrence compared to simple chemotherapy. It covers a wider range of treatment, enhances the recognition and killing of tumor cells, and improves the immune response. It is a very good treatment strategy [12].

4. An overview of tumor vaccines

Tumor vaccines are a new type of treatment method at present, and they have not been widely applied in clinical practice like other treatment methods such as chemotherapy. The main types of existing tumor vaccines include peptide/protein vaccines, cell vaccines, gene vaccines, and oncolytic vaccines, among which the vaccine types that can be used to treat breast cancer include protein/full-cell vaccines, nucleic acid vaccines, dendritic cell vaccines, and peptide vaccines [13,14]. For tumor vaccines targeting the treatment of TNBC, they are still in the clinical trial stage and no mature products have been approved for market release. However, some types of tumor vaccines have mechanisms similar to those for treating TNBC and are worthy of the author’s attention. Peptide

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vaccines stimulate the immune response by activating the immune system based on the fragments of the peptide antigens on the surface of tumor cells. They can also reduce the probability of recurrence [14].

Dendritic cell (DC) vaccines, after binding to tumor-specific antigens in vitro and then being re-administered to the patient, enhance the recognition and attack of tumor cells. Nucleic acid vaccines include DNA vaccines and RNA vaccines. Among them, RNA vaccines can induce the production of antigens in the body, thereby triggering an immune response [8].Therefore, the treatment of tumor vaccines is closely linked to their mechanisms. The vaccines contain tumor-related antigens (TAA or TSA), which are recognized by antigen-presenting cells such as dendritic cells (DCs) and presented to $CD8^+$ cytotoxic T cells and $CD4^+$ helper T cells to stimulate the immune response [15]. After the immune response is activated, B cells and antibodies are produced, and tumor vaccines help generate antibodies to stimulate the immune response and produce memory cells to reduce the probability of recurrence.

5. Advances in vaccine research for triple-negative breast cancer

Regarding the progress of TNBC vaccines, the advantages and disadvantages of the treatment methods are worthy of the author's attention and understanding. Currently, when TNBC vaccines are in the research stage, their research value mainly lies in several aspects. The specificity of the vaccine is stronger compared to other traditional treatment methods, and it can precisely target TNBC tumor cells by introducing antigens, causing less damage to normal cells compared to chemotherapy. The safety of vaccine treatment is higher. Traditional treatment methods such as chemotherapy have stronger toxicity, resulting in many side effects such as hair loss and bone marrow suppression, while the toxicity of vaccine treatment is lower, only causing limited adverse reactions, and improving the tolerance of patients [7,14].

According to the introduction of the above topic, vaccines can reduce the possibility of recurrence by stimulating immune responses and generating memory cells. Although tumor vaccines have many benefits for treating TNBC, they also have some disadvantages and challenges in the research process. TNBC has many different subtypes, which reflects the limitations of this treatment method and increases the challenges in research, making it difficult for researchers to develop a universal vaccine to cover all patients with TNBC. Different vaccines need to be developed, which may also lead to significantly increased costs [7]. Therefore, the use of vaccines to treat TNBC still requires continuous clinical trials and further research to ensure its safety and effectiveness.

6. Conclusion

Overall, although triple-negative breast cancer is the most severe subtype of breast cancer, patients still has many treatment options available for this type of cancer.In addition to the commonly used immunotherapy and chemotherapy, in recent years, there have also been many research advancements in using vaccines to treat TNBC. According to the explanation in this article, the safety and toxicity of using vaccines to treat TNBC are lower than those of chemotherapy, causing less harm to the human body, and also have a lower recurrence rate compared to immunotherapy.However, there are still some challenges in using vaccines for the treatment of TNBC. For instance, the diverse subtypes of TNBC make it difficult to develop a universal vaccine. Therefore, using vaccines for the treatment of TNBC has both benefits and challenges. Nevertheless, the author can still see that using vaccines for treatment is a promising and hopeful approach, and there is hope that vaccine therapy will become a common treatment for TNBC in the future.

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References

[1] Lei, S., Zheng, R., Zhang, S., Wang, S., Chen, R., Sun, K., Zeng, H., Zhou, J. and Wei, W. (2021) Global patterns of breast cancer incidence and mortality: A population-based cancer registry data analysis from 2000 to 2020. Cancer Communications, 41, 1183–1194.

[2] Livasy, C.A. (2009) Triple-negative breast cancer. Surgical Pathology Clinics, 2, 247-261.

[3] Schmid, P., Adams, S., Rugo, H.S., Schneeweiss, A., Barrios, C.H., Iwata, H., Diéras, V., Hegg, R., Im, S.A., Shaw Wright, G., Henschel, V., Molinero, L., Chui, S.Y., Funke, R., Husain, A., Winer, E.P., Loi, S. and Emens, L.A. (2018) IMpassion130 Trial Investigators. Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer. The New England Journal of Medicine, 379, 2108-2121.

[4] Medina, M.A., Oza, G., Sharma, A., Arriaga, L.G., Hernández Hernández, J.M., Rotello, V.M. and Ramirez, J.T. (2020) Triple-Negative Breast Cancer: A Review of Conventional and Advanced Therapeutic Strategies. International Journal of Environmental Research and Public Health, 17, 2078.

[5] Mahfoudh, W., Bettaieb, I., Ghedira, R., Snoussi, K., Bouzid, N., Klayech, Z., Gabbouj, S., Remadi, Y., Hassen, E., Bouaouina, N. and Zakhama, A. (2019) Contribution of BRCA1 5382insC mutation in triple negative breast cancer in Tunisia. Journal of Translational Medicine, 17, 123.

[6] Morse, M.A., Gwin, W.R. ranked 3rd. and Mitchell, D.A. (2021) Cancer Vaccine Therapy: Past and Present. OncoTargets and Therapy, 16, 121-152.

[7] Fines, C., McCarthy, H. and Buckley, N. (2025) The search for a TNBC vaccine: the guardian vaccine. Cancer Biology & Therapy, 26, 2472432.

[8] Gilmore, E., McCabe, N., Kennedy, R.D. and Parkes, E.E. (2019) DNA Repair Deficiency in Breast Cancer: Opportunities for Immunotherapy. Journal of Oncology, 2019, 4325105.

[9] Rosa, M.L., Reinert, T., Pauletto, M.M., Sartori, G., Graudenz, M. and Barrios, C.H. (2023) Implications of tumor-infiltrating lymphocytes in early-stage triple-negative breast cancer: clinical oncologist perspectives. Translational Breast Cancer Research, 5, 4.

[10] Korde, L.A., Somerfield, M.R., Carey, L.A., Crews, J.R., Denduluri, N., Hwang, E.S., Khan, S.A., Loibl, S., Morris, E.A., Perez, A., Regan, M.M., Spears, P.A., Sudheendra, P.K., Symmans, W.F., Yung, R.L., Harvey, B.E. and Hershman, D.L. (2021) Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline. Journal of Clinical Oncology, 39, 1485-1505.

[11] Huang, L., Lang, G.T., Liu, Q., Shi, J.X., Shao, Z.M. and Cao, A.Y. (2021) A predictor of pathological complete response to neoadjuvant chemotherapy in triple-negative breast cancer patients with the DNA repair genes. Annals of Translational Medicine, 9, 301.

[12] Cortes, J., Haiderali, A., Huang, M., Pan, W., Schmid, P., Akers, K.G., Park, J.E., Frederickson, A.M., Fasching, P.A. and O'Shaughnessy, J. (2023) Neoadjuvant immunotherapy and chemotherapy regimens for the treatment of high-risk, early-stage triple-negative breast cancer: a systematic review and network meta-analysis. BioMed Central Cancer, 23, 792.

[13] Palma, M. (2025) Advancing Breast Cancer Treatment: The Role of Immunotherapy and Cancer Vaccines in Overcoming Therapeutic Challenges. Vaccines, 13, 344.

[14] Poodineh, J., Sirati-Sabet, M., Rajabibazl, M. and Mohammadi-Yeganeh, S. (2020) MiR-130a-3p blocks Wnt signaling cascade in the triple-negative breast cancer by targeting the key players at multiple points. Heliyon, 6, e05434.

[15] Kaczmarek, M., Poznańska, J., Fechner, F., Michalska, N., Paszkowska, S., Napierała, A. and Mackiewicz, A. (2023) Cancer Vaccine Therapeutics: Limitations and Effectiveness-A Literature Review. Cells, 12, 2159.