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THE ROLE OF IMMUNOTHERAPY IN THE TREATMENT OF UTERINE AND CERVICAL CANCERS: EFFECTIVENESS, RECENT ADVANCES, AND APPLICATION METHODS

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Abstract: Uterine and cervical cancers remain major global health challenges, particularly in low- and middle-income countries where the incidence and mortality rates are disproportionately high. Despite advances in surgery, chemotherapy, and radiotherapy, treatment outcomes for advanced and recurrent disease remain unsatisfactory. Recent developments in immunotherapy, including immune checkpoint inhibitors, therapeutic vaccines, and adoptive cell transfer, have introduced promising new strategies in gynecologic oncology. Clinical trials demonstrate improved overall survival and durable responses in patients with PD-L1–positive and microsatellite instability-high (MSI-H) tumors. However, variability in response rates, immune-related toxicities, and economic barriers pose significant challenges to widespread clinical adoption. This article explores the current role, effectiveness, and limitations of immunotherapy in uterine and cervical cancers, highlights recent breakthroughs, and discusses future perspectives for integrating immunotherapy into multimodal treatment approaches.
Keywords: Uterine cancer; Cervical cancer; Immunotherapy; Immune checkpoint inhibitors; HPV vaccine; Adoptive T-cell therapy; PD-L1 expression; Microsatellite instability; Gynecologic oncology; Personalized medicine.

РОЛЬ ИММУНОТЕРАПИИ В ЛЕЧЕНИИ РАКА МАТКИ И ШЕЙКИ МАТКИ: ЭФФЕКТИВНОСТЬ, ПОСЛЕДНИЕ ДОСТИЖЕНИЯ И МЕТОДЫ ПРИМЕНЕНИЯ

Аннотация: Рак матки и шейки матки остаются серьёзной проблемой глобального здравоохранения, особенно в странах с низким и средним уровнем дохода, где показатели заболеваемости и смертности непропорционально высоки. Несмотря на достижения в хирургии, химиотерапии и лучевой терапии, результаты лечения запущенных и рецидивирующих форм заболевания остаются неудовлетворительными. Недавние разработки в области иммунотерапии, включая ингибиторы иммунных контрольных точек, терапевтические вакцины и адоптивный перенос клеток, открыли новые многообещающие стратегии в гинекологической онкологии. Клинические испытания демонстрируют улучшение общей выживаемости и стойкий ответ у пациентов с опухолями, положительными по PD-L1 и с высоким уровнем микросателлитной нестабильности (MSI-H). Однако вариабельность показателей ответа, иммуноопосредованная токсичность и экономические барьеры создают серьёзные препятствия для широкого клинического внедрения этих методов. В данной статье рассматриваются текущая роль, эффективность и ограничения иммунотерапии при раке матки и шейки матки, освещаются недавние достижения и обсуждаются перспективы интеграции иммунотерапии в мультимодальные подходы к лечению.

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Ключевые слова: Рак матки; Рак шейки матки; Иммунотерапия; Ингибиторы контрольных точек иммунитета; Вакцина против ВПЧ; Адоптивная Т-клеточная терапия; Экспрессия PD-L1; Микросателлитная нестабильность; Онкогинекология; Персонализированная медицина.

Introduction

Uterine and cervical cancers remain among the most prevalent malignancies affecting women worldwide, representing a major burden on public health and clinical practice. Despite significant progress in screening programs, surgical approaches, chemotherapy, and radiotherapy, mortality rates from these cancers remain substantial, especially in low- and middle-income countries. Conventional treatments often face limitations due to tumor resistance, systemic toxicity, and recurrence, which necessitates the exploration of innovative therapeutic strategies. In recent years, immunotherapy has emerged as a promising approach in oncology, including gynecological cancers. Unlike traditional methods that directly target tumor cells, immunotherapy focuses on modulating the patient's immune system to recognize and eliminate malignant cells. This therapeutic strategy includes immune checkpoint inhibitors, cancer vaccines, adoptive cell transfer, and monoclonal antibodies, each offering new prospects for durable responses and improved survival rates.

The application of immunotherapy in uterine and cervical cancers is supported by advances in molecular biology and tumor immunology, which have clarified the role of immune evasion mechanisms in cancer progression. The introduction of immune checkpoint inhibitors, such as PD-1/PD-L1 and CTLA-4 blockers, has already shown encouraging results in clinical trials. Furthermore, the combination of immunotherapy with conventional treatments has been investigated to enhance therapeutic outcomes and overcome resistance mechanisms. Given the rapid development of this field, it is crucial to assess the current effectiveness of immunotherapy, evaluate recent innovations, and review methodological approaches to its clinical application. This paper aims to provide a comprehensive analysis of immunotherapy in the management of uterine and cervical cancers, highlighting both achievements and challenges, as well as outlining perspectives for its integration into routine clinical practice.

Main part

Immunotherapy has emerged as one of the most promising treatment modalities in modern oncology, particularly in gynecologic cancers such as uterine and cervical malignancies. Unlike conventional approaches like chemotherapy and radiotherapy, which directly target tumor cells, immunotherapy focuses on enhancing the patient's immune system to recognize and eradicate cancer cells. This paradigm shift has changed the overall outlook for patients with advanced or recurrent disease, where traditional therapies have shown limited success. Cervical cancer, being strongly associated with persistent human papillomavirus (HPV) infection, provides a unique immunological landscape where targeted immunotherapeutic agents can demonstrate significant clinical benefit. Similarly, endometrial cancer, which often arises in the context of genetic mutations and microsatellite instability, has been shown to be responsive to immune checkpoint inhibitors. In this context, immunotherapy not only broadens the therapeutic arsenal but also offers the potential for durable responses and improved quality of life.

The scientific rationale for applying immunotherapy in cervical and uterine cancers lies in their underlying molecular and immunological characteristics. Cervical cancer is largely caused by HPV, which integrates viral oncoproteins such as E6 and E7 into host cells, leading to uncontrolled cell proliferation and immune evasion. These viral antigens act as potential targets for immune-based treatments. On the other hand, uterine cancers, especially those with

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microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR), generate numerous neoantigens that make them particularly immunogenic. The tumor microenvironment in both cancers, however, is characterized by immune suppressive factors, such as increased regulatory T cells, tumor-associated macrophages, and expression of programmed death ligand-1 (PD-L1). Immunotherapy aims to overcome these mechanisms of immune evasion, enabling cytotoxic T lymphocytes to effectively attack tumor cells. Thus, the pathophysiological background strongly supports the application of novel immunotherapeutic strategies in these gynecological malignancies.

The main therapeutic strategies in immunotherapy for these cancers include immune checkpoint inhibitors, therapeutic vaccines, adoptive T-cell therapies, and cytokine-based treatments. Immune checkpoint inhibitors target inhibitory pathways such as PD-1/PD-L1 and CTLA-4, restoring the ability of T cells to identify and destroy cancer cells. Therapeutic vaccines, particularly those targeting HPV antigens, aim to induce a robust and specific immune response against infected or transformed cells. Adoptive T-cell therapy, including tumor-infiltrating lymphocytes (TILs), has shown promising results in early trials, where patient-derived T cells are expanded ex vivo and reinfused to mount a stronger antitumor response. Cytokine therapies attempt to enhance immune cell proliferation and activity by using molecules such as interleukin-2. These mechanisms highlight the multifaceted approach of immunotherapy, which can be personalized depending on the molecular and immunological profile of each patient's tumor.

Clinical trials over the past decade have demonstrated significant progress in the use of immunotherapy for uterine and cervical cancers. In cervical cancer, immune checkpoint inhibitors such as pembrolizumab have been approved for patients with PD-L1 positive tumors, showing durable responses in a subset of patients. In uterine cancers with MSI-H or dMMR, checkpoint inhibitors like dostarlimab and pembrolizumab have shown remarkable efficacy, often outperforming traditional therapies. Clinical evidence suggests that while not all patients respond, those who do achieve long-lasting remission, which is rarely seen with chemotherapy. Importantly, immunotherapy can also be combined with other modalities, including chemotherapy and radiation, to enhance overall survival outcomes. However, challenges remain, particularly in identifying biomarkers that predict response and in managing immune-related toxicities. Overall, immunotherapy has transitioned from experimental treatment to a mainstream therapeutic option in certain patient populations.

Recent innovations in immunotherapy have expanded the therapeutic potential in uterine and cervical cancer. One of the most notable advances is the development of personalized cancer vaccines targeting specific tumor neoantigens, which can be designed using genomic sequencing. Additionally, novel immune checkpoint inhibitors and combination regimens are being explored, including dual blockade of PD-1 and CTLA-4. Advances in adoptive T-cell therapy, such as genetically engineered T-cell receptors (TCRs) and chimeric antigen receptor T-cell (CAR-T) therapies, have opened new horizons for treatment-resistant cases. Furthermore, ongoing research into tumor microenvironment modulation aims to enhance the efficacy of immunotherapy by overcoming immunosuppressive barriers. Artificial intelligence and biomarker discovery are also accelerating the identification of patients most likely to benefit. These innovations reflect the dynamic and rapidly evolving field of cancer immunotherapy. The practical application of immunotherapy involves careful patient selection, biomarker testing, and administration protocols. PD-L1 expression testing and MSI/MMR profiling are now standard practices before prescribing immune checkpoint inhibitors. Administration is generally done via

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intravenous infusion at regular intervals, with treatment duration depending on response and tolerability. Combination therapies, such as immunotherapy with chemotherapy or radiotherapy, require multidisciplinary coordination to optimize outcomes. Additionally, patient monitoring is essential to evaluate tumor response, detect adverse events, and decide whether therapy should be continued or discontinued. In resource-limited settings, cost and accessibility remain significant challenges, requiring adaptation of methodologies. The integration of immunotherapy into existing treatment algorithms demonstrates the shift towards personalized and precision medicine in oncology.

Despite its promise, immunotherapy is not without limitations. Response rates remain variable, with many patients showing primary or acquired resistance to treatment. Immune-related adverse events, such as colitis, pneumonitis, and endocrinopathies, can significantly impact patient safety and require specialized management. Additionally, the high cost of immunotherapy restricts its accessibility, particularly in low- and middle-income countries where the burden of cervical cancer is highest. Biomarker discovery remains a critical challenge, as current predictors like PD-L1 expression are imperfect and do not fully explain treatment response. Moreover, the optimal duration of therapy, sequencing with other treatments, and long-term effects remain areas of active investigation. These challenges highlight the need for continued research and refinement of immunotherapeutic strategies.

The future of immunotherapy in uterine and cervical cancers is promising, with ongoing research expected to refine current practices and expand therapeutic opportunities. Combination strategies with targeted therapies, hormonal treatments, and novel agents are anticipated to further improve response rates. The integration of personalized medicine, guided by genomic and immunologic profiling, will likely enhance treatment precision and effectiveness. Furthermore, global health initiatives are needed to ensure equitable access, particularly in regions where cervical cancer remains a leading cause of mortality. Continued investment in clinical trials, translational research, and technological innovation will be crucial in shaping the next generation of cancer treatment. In conclusion, immunotherapy represents a transformative approach in gynecologic oncology, offering hope for improved survival and quality of life in patients with uterine and cervical cancers.

Discussion and Results

The clinical implementation of immunotherapy in uterine and cervical cancers has shown both encouraging benefits and notable limitations. Recent findings indicate that immune checkpoint inhibitors, such as pembrolizumab and nivolumab, can significantly improve overall survival and progression-free survival in selected groups of patients, especially those with PD-L1–positive tumors and microsatellite instability-high (MSI-H) profiles. These outcomes underline the critical role of tumor immunogenicity in predicting treatment response. The integration of immunotherapy with conventional treatments such as chemotherapy and radiotherapy has produced synergistic effects, enhancing the efficacy of treatment regimens and extending the duration of disease control. Moreover, therapeutic HPV vaccines have demonstrated substantial promise, not only as preventive strategies but also as potential therapeutic tools for patients with recurrent cervical malignancies.

Nevertheless, the results also reveal key challenges that need to be addressed. Response rates remain highly variable, with some patients experiencing durable remission while others show minimal benefit. This heterogeneity suggests that additional research is necessary to refine biomarker-based patient selection. Furthermore, immune-related adverse events, ranging from mild dermatologic conditions to severe autoimmune complications, remain a significant clinical

AMERICAN ACADEMIC PUBLISHER
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concern and require specialized management protocols. Economic considerations are another barrier, as immunotherapy treatments remain expensive and less accessible in low-resource settings, despite the disproportionately high incidence of cervical cancer in such regions. Overall, the findings suggest that immunotherapy represents a transformative but still developing approach in gynecologic oncology. While not a universal solution, it provides durable benefits for specific patient subgroups and has the potential to reshape the future of cancer care when combined with personalized medicine and advanced clinical strategies. Continued investigation into predictive biomarkers, optimized treatment combinations, and cost-effective applications will be essential to maximize its impact on patient outcomes.

References

1. Bhatla, N., Aoki, D., Sharma, D. N., & Sankaranarayanan, R. (2018). Cancer of the cervix uteri. *International Journal of Gynecology & Obstetrics*, 143(Suppl 2), 22–36.
2. Cohen, P. A., Jhingran, A., Oaknin, A., & Denny, L. (2019). Cervical cancer. *The Lancet*, 393(10167), 169–182.
3. Бабажанова, Ш. Д., Любчич, А. С., & Джаббарова, Ю. К. (2021). Факторы, способствовавшие неблагоприятному исходу при преэклампсии. *Фундаментальная и клиническая медицина*, *6*(1), 27-31.
4. Bacci, A., Hodorogea, S., Khachatryan, H., Babojonova, S., Irsa, S., Jansone, M., ... & Lazzerini, M. (2018). What is the quality of the maternal near-miss case reviews in WHO European Region? Cross-sectional study in Armenia, Georgia, Latvia, Republic of Moldova and Uzbekistan. *BMJ open*, *8*(4), e017696.
5. Babazhanova, S. D., Lyubchich, A. S., & Lyubchich, N. I. (2022). Efficacy of using controlled uterine balloon tamponade for stopping atonic postpartum hemorrhage. *Journal of obstetrics and women's diseases*, *71*(1), 5-10.
6. Chung, H. C., Ros, W., Delord, J. P., Perets, R., Italiano, A., Shapira-Frommer, R., ... & Leary, A. (2019). Efficacy and safety of pembrolizumab in previously treated advanced cervical cancer: Results from the phase II KEYNOTE-158 study. *Journal of Clinical Oncology*, 37(17), 1470–1478.
7. Бабажанова, Ш. Д. (2009). Исходы при фетоплацентарной недостаточности различной степени тяжести в зависимости от акушерской тактики. *Врач-аспирант*, *37*(10), 910-914.
8. Colombo, N., Dubot, C., Lorusso, D., Caceres, M. V., Hasegawa, K., Shapira-Frommer, R., ... & Leary, A. (2021). Pembrolizumab for persistent, recurrent, or metastatic cervical cancer. *New England Journal of Medicine*, 385(20), 1856–1867.