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Immunotherapy in the Treatment of Gynecologic Malignancies

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EDITORIAL

It has long been hypothesised that the immune system has a role in ovarian cancer. T cell infiltration of tumours is an independent predictive factor for overall survival in advanced ovarian cancer, according to multivariate analysis. The immune response's phenotype has been found to be important; CD8+ T cell infiltration of tumours has been linked to a better prognosis, whilst regulatory T cells and myeloid-derived suppressor cells have been linked to a worse prognosis. This is further confirmed by data from The Cancer Genome Atlas project, which shows that among high-grade serous ovarian tumours, the immunoreactive-like subtype had the greatest survival profile.

Because ovarian tumours are immunogenic, understanding ways to modify the immune response to enhance prognosis has been a focus of research. Understanding how immune variables influence or are influenced by chemotherapy and surgery, as well as how immune therapies might be integrated into current treatment paradigms, are becoming increasingly essential considerations. In the context of neoadjuvant chemotherapy and surgical result in high-grade serous ovarian cancer, these issues have been looked into further. Tumor infiltration by T cells did not continue to be associated with a better prognosis in patients treated with neoadjuvant chemotherapy, whereas CD8 + T cells were associated with a better prognosis only when cytoreduction to no residual disease was achieved, but not in patients who were cytoreduced optimally (b1 cm) or incompletely.

IMMUNOTHERAPY

Monoclonal antibodies targeting the PD-1/PD-L1 pathway have shown promise in stimulating immune responses against malignancies through immune checkpoint inhibition. The PD1/PD-L1 connection is a natural process that prevents autoimmunity, but cancers use it to elude the immune system. In high-grade serous ovarian tumours, PD-L1 expression has been linked to a better prognosis. Nivolumab, an anti-PD-1 monoclonal antibody, showed 15% response rates and a 20-month overall survival rate in platinum-resistant ovarian cancer patients with low side effects. Pembrolizumab, a monoclonal antibody that targets PD-1, and avelumab, a monoclonal antibody that targets PD-L1, have shown similar outcomes. Ovarian cancer therapeutic vaccines are also being investigated. To treat advanced ovarian cancer, vaccinations have recently been used with cytotoxic chemotherapies. This has been prompted by the discovery that cytotoxic chemotherapies used to treat ovarian cancer may work in tandem with immune-based treatments. Antigen-specific T cell responses were induced by peptide vaccination targeting p53 in conjunction with gemcitabine and interferon, which raised circulating CD4+ and CD8+ T cells without boosting regulatory T cells. In advanced ovarian cancer patients, peptide immunisation targeting survivin in combination with metronomic cyclophosphamide has also been found to be immunogenic and capable of creating polyfunctional T cells [1-5].

TREATMENT

Immunotherapies that have shown potential in the treatment of other cancers will be examined for ovarian cancer. Ovarian cancer patients have received adoptive T cell therapy employing chimeric antigen receptors (CAR-T cells) that target mesothelin. Chemotherapies combined with immunomodulatory antibodies are also being researched. Bringing these ideas to ovarian cancer could lead to immune treatments being used

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in adjuvant, maintenance, or neoadjuvant settings, rather than just for recurrent illness.

Immunotherapies for gynecologic malignancies are still being developed at a rapid pace. Tumor biology research and genetic analysis will provide improved vaccination and T cell treatment targets. It will be possible to build sensible combinations of therapies to boost responses by better understanding the mechanisms of current immunotherapies as well as the immunologic effects of radiation and cytotoxic chemotherapy. New immunotherapies will be able to target patients who are most likely to benefit thanks to biomarkers linked to response. Immunotherapy for gynecologic cancers may soon achieve its potential, with medicines prepared to tackle pathways long utilised by tumours to disrupt anti-tumor responses.

CONCLUSION

Immunotherapies for gynecologic malignancies are still being developed at a rapid pace. Tumor biology research and genetic analysis will provide improved vaccination and T cell treatment targets. It will be possible to build sensible combinations of therapies to boost responses by better understanding the mechanisms of current immunotherapies as well as the immunologic effects of radiation and cytotoxic chemotherapy. New immunotherapies will be able to target patients who are most likely to benefit thanks to biomarkers linked to response. Immunotherapy for gynecologic cancers may soon achieve its potential, with medicines prepared to tackle pathways long utilised by tumours to disrupt anti-tumor responses.

CONFLICT OF INTEREST

None.

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