Presurgery chemotherapy may make advanced ovarian cancers responsive to immunotherapy

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Bottom Line: Metastatic ovarian cancer patients treated with chemotherapy prior to surgery had altered immune cells in their tumors, and specific alterations identified suggest that immunotherapy given after chemotherapy may help in preventing the cancer from coming back.

The study is published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research, by Frances R. Balkwill, PhD, professor of cancer biology at Barts Cancer Institute in Queen Mary University of London, United Kingdom.

"We are studying a type of ovarian cancer called high-grade serous ovarian cancer (HGSC), which is quite difficult to treat for two main reasons: first, it is often detected after it has spread quite extensively in the body; and second, although the disease can respond well to the first chemotherapy treatments, it often relapses and becomes more difficult to treat. Therefore we need to find other treatment options after the initial treatment is given," said Balkwill.

Prior preclinical research in mice suggests that when chemotherapy destroys cancer cells, it also stimulates immune cells in the cancer that can kill cancer cells, she explained. "We wanted to study whether this was also true in cancer patients, and whether it occurred with the chemotherapy used to treat women with ovarian cancer," Balkwill added.

Balkwill and colleagues collected pre- and post-chemotherapy biopsies and blood samples from 54 patients with advanced-stage HGSC who underwent platinum-based neoadjuvant (given prior to surgery) chemotherapy, and from six patients who underwent surgery without prior chemotherapy.

The researchers analyzed the samples using immunohistochemistry and RNA sequencing to study the changes in the tumor immune microenvironment of patients who received and did not receive chemotherapy, and changes before and after chemotherapy. Patients were categorized into those who had a good response and those who had a poor response to chemotherapy, based on a recently approved chemotherapy response score that correlates with progression-free and overall survival.

They found that in patients who received chemotherapy, there was evidence of activation of certain types of T cells that can fight cancer cells, while the number of a type of T cell that suppresses the immune system decreased. The results were more pronounced in those who had a good response to chemotherapy, compared with those who had a poor response to chemotherapy.

The team also found that chemotherapy reduced the blood levels of certain cytokines—inflammatory molecules that promote cancer growth—often back to normal levels in the patients. "This could help immunotherapies work better," Balkwill noted.

"Our study showed that chemotherapy altered the immune cells called T cells that are found in metastatic ovarian cancer samples in a way that suggested they were better able to fight the cancer after the treatment. Our research provides evidence that immunotherapy may be more effective if given straight after chemotherapy," Balkwill said.

"Although we found that chemotherapy activated the T cells, the levels of the protein PD-L1 [to which the immune checkpoint molecule PD-1 binds to disable T cells and prevent them from recognizing and destroying the cancer cells] remained the same or increased. However, immune checkpoint

blockade therapies [such as pembrolizumab and nivolumab] can stop this from happening, so we suggest that immune checkpoint blockade might be a suitable form of immunotherapy to give to ovarian cancer patients after chemotherapy," she added.

"The chemotherapies, carboplatin and paclitaxel, given in our study are also used to treat many different cancer types. It will, therefore, be very interesting and potentially promising if similar effects are seen in other cancer types, such as lung cancer," Balkwill noted.

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