Interleukin-6 and cancer risk

Under certain situations, such as the very early stages of an infection (called an acute infection), the immune system produces chemical signals, or cytokines, to help the body cope with this infection. One such cytokine is interleukin-6 (IL-6). During the acute stage of an infection, relatively high levels of IL-6 are produced and this, together with other cytokines, helps to activate T-cells, increase the number of antibody-producing B-cells and stimulate the release of hormones. Such a response during an acute infection is likely useful. However, prolonged production of relatively high levels of IL-6 may weaken the immune system over the long-term. This weakness can occur because higher-than-normal levels of IL-6 can cause the premature death of immune cells, increase the susceptibility of the liver to injury and raise the risk for cardiovascular disease. Some studies in people have found a link between an elevated level of IL-6 and an increased risk for the growth of tumours.

Chronically high levels of IL-6 might also play a role in weakening the immune systems of HIV-positive people. To investigate this possibility, researchers with the Insight Research Network, which links doctors and scientists across North America, Western Europe and Australia, reviewed information in their database. Specifically, they focused on 5,000 HIV-positive people who had been monitored for several years as part of clinical trials; apart from ART, they did not receive any other treatment. In assessing several proteins associated with inflammation—IL-6, D-dimer and C-reactive protein—a 40% increased risk for cancer was associated with elevated IL-6 levels.

Study details

Researchers reviewed data from 5,023 HIV-positive people. All participants had been randomly assigned to the control arms of several clinical trials—Esprit, Silcaat and Smart—and, apart from ART, did not receive additional interventions such as interleukin-2 or structured treatment interruptions.

The average profile of participants when they entered the studies was as follows:

- 80% men, 20% women
- age – 40 years
- CD4+ count – 400 cells
- viral load – undetectable

Participants were monitored for seven years.

Results

Statistical analysis found that participants with elevated IL-6 levels in their blood had the strongest risk for developing cancer. This link between IL-6 and cancer risk persisted throughout the study and was associated with all cancers studied.

There were a total of 172 cancers that occurred in the IL-6 study, 101 of which were caused by viral infections such as the following:

- EBV – Epstein Barr Virus; linked to the development of lymphoma
- HBV – hepatitis B virus; this can cause liver cancer
- HCV – hepatitis C virus; this can cause liver cancer
- HPV – human papilloma virus; this can cause many cancers such as those of the anus, cervix, mouth, throat, penis, vulva and vagina

The most common cancers were as follows:
• infection-related cancers: anal cancer and lymphoma
• non-infection-related cancers: lung, colon and prostate cancers

The research team suspects that aging is probably driving the increase in IL-6 and cancer risk seen in its study.

Note that the present analysis was based on studies of stored blood samples collected for another purpose. Therefore, its findings are not definitive. However, the relatively large number of participants and the long period of monitoring suggest that its findings are important and intriguing. The next step in uncovering more about the role of IL-6 and cancer risk in HIV infection is to plan and conduct a study of a different design to confirm the findings of the Insight analysis. If the link between IL-6 and increased cancer risk is confirmed, then clinical trials of therapies designed to decrease IL-6 levels could be one possible way to explore reducing the elevated risk of cancer associated with HIV infection.

—Sean R. Hosein

REFERENCES:

Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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