Study Suggests Testosterone Suppresses Brain Tumor Growth

Findings from the NIH-funded study may warrant exploration of the hormones as glioblastoma treatment.

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In a new National Institutes of Health (NIH)-funded study, scientists at Cleveland Clinic discovered that hormones associated with male development may play a key role in limiting the growth of brain tumors in men.

The research team found that the loss of androgen hormones, such as testosterone, in a preclinical model of glioblastoma drove tumor growth by inducing local inflammation and triggering the production of stress hormones. In an analysis of data from more than 1,300 men with glioblastoma, the authors found that supplemental testosterone was significantly associated with improved survival, which was consistent with their preclinical experiments.

“This outcome is a welcome surprise and may potentially offer a lead for new treatments for a kind of cancer that is deadlier in men,” said Anthony Letai, MD, PhD, director of NIH’s National Cancer Institute (NCI).

As glioblastoma and androgens are simultaneously of higher prevalence in men, many researchers have suspected that these hormones are part of the problem. However, previous studies have not investigated the effects of androgens on tumor growth in the unique environment of the brain.

“The brain has evolved to keep stuff out and that includes immune cells from elsewhere in the body. It’s a delicate tissue that often doesn’t want huge immune reactions,” said corresponding author Justin Lathia, PhD, a professor of cancer sciences and scientific director of the Brain Tumor Center at Cleveland Clinic.

Lathia and his colleagues discovered that androgens in the brain play a crucial role in regulating the organ’s security systems, unlike other places in the body. Reducing androgens in mouse models of glioblastoma put a neuroendocrine system called the hypothalamus-pituitary-adrenal (HPA) axis into overdrive. This caused a spike in stress hormones that subsequently drove a subset of cells to further insulate the brain from the rest of the body.

The tightened security created an immunosuppressive environment in the brain, meaning fewer

immune cells could reach the growing threat and thus, tumors progressed mostly unchecked. The authors found that testosterone did not produce the same effect in female mice.

The researchers identified that the HPA axis is likely triggered by inflammation in the hypothalamus caused by tumors in androgen-deficient mice. In future work, they intend to pin down exactly how tumors can induce this reaction in an entirely separate region of the brain.

Seeking to explore the relationship between androgens and brain cancer in humans, the researchers analyzed existing clinical data made available through the NIH/NCI Surveillance, Epidemiology, and End Results (SEER) database. They found that men with glioblastoma who were receiving supplemental testosterone for reasons unrelated to cancer demonstrated a 38% lower risk of death compared to patients not taking the same supplements.

Though not establishing a causal relationship, Lathia and his colleagues believe this observational finding together with their preclinical results warrant clinical trials for further investigation in humans.

“An obvious follow-up study would be to find out whether androgen deprivation, which is a common treatment for cancer, is actually detrimental for glioblastoma,” Lathia said.

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