Maternal stress increases development of fetal neuroblastoma in animal model

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While genetics play a substantial role in development of neuroblastoma, scientists say that something else is in play that elevates the risk: stress.

Researchers from Georgetown University Medical Center have shown in mice genetically predisposed to develop neuroblastoma that maternal stress can push onset of the cancer. Their study will be presented at the American Association for Cancer Research (AACR) Annual Meeting 2015.

"To our knowledge, this is the first evidence of the role of prenatal stress in development of neuroblastoma," says Joanna Kitlinska, PhD, assistant professor in the department of biochemistry and molecular & cellular biology at Georgetown University Medical Center.

"We're far from saying that prenatal stress causes neuroblastoma by itself in people," she says. "But it appears, at least in animals, that prenatal stress can exacerbate the effect of underlying genetic aberrations that promote neuroblastoma development."

Neuroblastomas are the most common solid cancer in infants and very young children. Since neuroblastomas arise very early in life, often in infancy or even in the fetus, it makes sense that exposure to environmental factors promoting neuroblastoma occur during pregnancy or even before conception, Kitlinska says.

Neuroblastomas arise from a defect in normal fetal neuronal

development, and can occur anywhere in the sympathetic nervous system - the system that governs the fight-or-flight stress response.

Kitlinska and her team tested the hypothesis that prenatal stress plays a role in the development of neuroblastoma because both hypoxia (low oxygen) and glucocorticoids have been known to alter normal neuronal development and increase aggressiveness of these tumors. Both are stress responses—in pregnant women cortisol (glucocorticoids) can cross the placenta and affect a fetus directly, and adrenalin, produced by stress, can cause restriction in maternal blood vessels, reducing oxygen to a fetus, she says.

In this study, the researchers looked at whether introducing glucocorticoids in pregnant mice (by implanting pellets containing the hormone) could promote neuroblastoma. Without any intervention, 32 percent of the control transgenic mice will develop the tumor.

Half of the mice were given pellets of glucocorticoids, and the other half placebo pellets. But an unintended finding emerged: the mere stress of handling the mice in the study—drawing blood several times and the use of anesthesia and surgery to insert pellets in the experimental group—appears to have increased the rate of fetal cancer development, whether or not they had been given glucocorticoids. In both groups, 64 percent of the pups developed neuroblastoma and the spread of the cancer was faster than in mice not subjected to the stress.

"If confirmed by further studies, this new paradigm will enhance our understanding of neuroblastoma etiology. It may also result in designing the first-ever preventative approaches for neuroblastoma," Kitlinska says.

More information: Prenatal stress increases NB tumorigenicity in TH-MYCN mice, American Association for Cancer Research (AACR)

Annual Meeting 2015

Provided by Georgetown University Medical Center