The Effect of Methotrexate Treatment on Neuroinflammation
Gene Expression in Pediatric Cancer Patients

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Background

Pediatric cancer survivors often experience long-lasting health consequences from their chemotherapy treatment. These deficits, termed late effects, are sequelae that arise months or years after a disease is identified or treatment has been completed.

Various types of therapy include:
- Surgery
- Bone marrow transplantation
- Radiation therapy
- Chemotherapy

Results found in literature:
- Mice in chemotherapy group showed impaired learning versus controls.
- Glial cell histology indicated differences in white but not grey matter in mouse and human tissue.
- White matter contains few cell bodies and primarily long-range myelinated axons.
- Decreased myelination may underpin learning impairment via interruption of normal oligodendrocyte and other glia development.

Methotrexate

The chemotherapy agent most used for the treatment of pediatric leukemias, and lymphomas is methotrexate, a synthetic folic acid antagonist. MTX indirectly inhibits cell division through the blockage of folate-related enzymes.

Methotrexate treatment in pediatric patients has been associated with the long-lasting development of detrimental neurological and psychosocial sequelae following cancer survival.

Project goals

Hypothesis: methotrexate treatment causes abnormal gene expression in neuroinflammation genes in the white matter and changes in neurological and psychosocial development in children.

Goals:
- Provide information regarding gene-environment interactions and thus reveal candidate risk genes and pathways contributing to neurocognitive and psychiatric late effects.
- Our research is incredibly important because the evaluation of genetic differences in cancer patients has not previously been evaluated. The long-term goal of this project is to improve the health outcomes and quality of life of cancer survivors.

Specific aim 1: Retrospective study of cancer survivors

- The patient charts will be reviewed retrospectively from the Late Effects Center at Children's Hospital of New Orleans, LA (CHNO).
- The clinic follows patients two years post-chemotherapy to evaluate any changes in neurological, visual, hearing, learning, motor skills, and other developmental outcomes up to the age of 22 years.

Specific aim 2: Genetic analysis of deceased cancer patients

- Evaluation of gene expression of known neuroinflammation genes on white matter samples from deceased patients who received methotrexate.
- Epidemiological data will be obtained from the patient charts to determine information regarding age of treatment, type and severity of cancer, length of treatment, and neurological and psychosocial effects.

Methods

- Methods of cancer patients, we can help improve the quality of life of childhood cancer survivors.

Conclusions

- Not only will the findings of our study be important to future research, but it will also be essential to physicians who provide late effects care so that they may tailor their treatments to each specific patient, their cancer, its treatment, and the late effects they experience. By creating a better understanding of late effects in pediatric cancer patients, we can help improve the quality of life of childhood cancer survivors.

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