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GMCSF treatment associated with improved cognition in cancer patients

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Growth factors shown to cure Alzheimer's disease in a mouse model and administered to cancer patients as part of their treatment regimen were linked to significant improvements in the patients' cognitive function following stem cell transplantation, a preliminary clinical study reports.

The findings by researchers at the USF Health Byrd Alzheimer's Institute and Moffitt Cancer Center are reported online in Brain Disorders *& Therapy*.

The retrospective study showed that cancer patients treated with granulocyte macrophage colony stimulating factor (GMCSF) plus granulocyte colony stimulating factor (GCSF) experienced greater improvement in memory and thinking than those treated with GCSF alone.

In the new study, the USF and Moffitt researchers investigated the link between GMCSF and cognitive functioning in humans for the first time, said principal investigator Huntington Potter, PhD, professor of molecular medicine at the USF Health Byrd Alzheimer's Institute. While the research looked at changes in cognition related to cancer treatment, it provided the basis for a new randomized controlled trial at the Byrd Alzheimer's Institute testing the safety and effectiveness of GMCSF (the drug sargramostim) in 40 patients with mild to moderate Alzheimer's disease.

GMCSF and GCSF, routinely administered to patients undergoing

transplants to treat blood or bone marrow cancers, have a proven safety track record for this use. These growth, or colony stimulating, factors boost blood-forming stem cells circulating in the patient's own blood before the cells are harvested for autologous hematopoietic cell transplantation (HCT), speed the repopulation of cells depleted by chemotherapy or radiation, and/or fight infection in patients receiving bone marrow or blood stem cells from a donor.

Those involved in cancer research and clinical care are aware that problems with memory and concentration, referred to as "chemo brain," can be a side effect of high-dose chemotherapy, which is part of the regimen accompanying HCT.

Previous University of South Florida (USF) studies by Dr. Potter, Tim Boyd, PhD, and others investigated GMCSF and GCSF separately in mice bred to develop symptoms of Alzheimer's disease. They showed that these growth factors both reduce beta amyloid, a substance forming the hallmark plaques in the brain associated with Alzheimer's, and reverse memory impairment, with GMCSF being more effective.

"This preliminary work is an intriguing first step and points to the importance of collaboration between different health disciplines," said lead author Heather Jim, PhD, assistant professor in the Health Outcomes and Behavior Department at Moffitt. "While more research is needed, the study suggests that GMCSF, a drug with a relatively good safety profile, may be able to either prevent or reverse cognitive decline not only in Alzheimer's patients, but cancer patients as well."

The USF-Moffitt study involved 19 cancer patients who received GMCSF and GCSF, and 76 who received GCSF only. No patients received GMCSF only. Most were diagnosed with multiple myeloma or non-Hodgkin's lymphoma and treated with autologous HCT.

Neuropsychological tests of memory, attention and executive function (complex thinking) conducted before patients received GMCSF and/or GCSF for treatment with HCT indicated significant cognitive impairment in all study participants. The same tests six months after HCT showed that group of patients administered GMCSF and GCSF performed significantly better than the group receiving GCSF only – in the area of memory improvement. By 12 months, there were no differences; both groups had improved significantly in memory and executive function.

"The GMCSF was associated with faster cognitive recovery," Potter said.

The finding that GMCSF plus GCSF was associated with initially greater cognitive improvement than GCSF alone may reflect GMCSF's ability to mobilize a broader range of cell types, particularly the recruitment of more immune cells known as microglia that rush to damaged or inflamed areas to get rid of toxic substances, Potter said.

"Although preliminary and retrospective," he added, "the current data indicate that colony stimulating factors, particularly GMCSF, should be further tested as cognition enhancers for a number of different indications, including cancer and neurodegenerative disease."

Provided by University of South Florida