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Identification of central nervous system involvement for patients with AIDS-related lymphomas

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Patients with AIDS-related lymphomas (ARL) may face an increased risk of central nervous system involvement (CNSi) compared to other lymphomas. The effect of CNSi on survival outcomes, however, hasn't been thoroughly examined until now.

In a new study led by Fox Chase Cancer Center Hematologist and Oncologist Stefan K. Barta, MD, MS, MRCP, researchers report that CNSi – identified at the time of an ARL diagnosis – does not appear to have an impact on overall survival. Dr. Barta's collaborators will present the findings at the 50th Annual Meeting of the American Society of Clinical Oncology.

In the same study, he and his team found that patients with CNSi at the time of diagnosis were nearly three times as likely, on average, to have CNS relapse (CNSr) during cancer treatment. CNSr is generally associated with particularly poor prognosis.

"It occurs early and usually has a poor outcome, though there are long term survivors," said Dr. Barta. He hopes a better understanding of how CNS involvement affects prognosis could lead to improvements in diagnostic tools and treatments.

Infection with human immunodeficiency virus, or HIV, greatly increases a person's risk of being diagnosed with many lymphomas. AIDS-related

lymphomas (ARL), which include diffuse large cell lymphomas and small noncleaved cell lymphomas, are particularly aggressive forms of disease. The vast majority of patients—at least 80 percent, according to the National Cancer Institute—have stage IV disease at the time of presentation. The central nervous system is among the most common sites outside the lymph nodes that may be involved with ARL.

In 2013, as part of a study on factors that influence outcomes for patients with ARL, Dr. Barta led the assembly of a database containing medical data from more than 1500 patients newly diagnosed with AIDS-related lymphomas who participated in clinical trials in Europe and the United States between 1990 and 2010, inclusive.

In the new study, he and his colleagues used the same database to identify 880 patients with ARL whose data included complete information on central nervous system involvement (CNSi) at diagnosis and relapse (CNSr).

They analyzed data to identify associations between CNSr and a variety of patient characteristics, including age, sex, CD4 count, treatment history with cART, lymphoma subtype, rituximab use, and type of initial chemotherapy. Only CNSi conferred a higher risk of relapse.

CNSi was identified in 13 percent of all 880 patients at the time of diagnosis, including 27 percent of patients with Burkitt Lymphoma or Burkitt-like lymphoma and 6 percent in patients with diffuse large B-cell lymphoma. Dr. Barta and his colleagues found that 5.3 percent of patients experienced CNSr a median of 4.2 months after diagnosis; those patients had a median overall survival of 1.6 months.

Sixty-nine percent—607 patients—had been treated with combination anti-retroviral therapies, or cART. These therapies, which came into use in 1996, reversed the dismal survival rates for patients with full-blown

AIDS and slowed the onset of AIDS for patients infected with HIV. However, Dr. Barta and his team found that cART did not reduce the frequency of CNSr in patients diagnosed with ARL. Neither did other treatments the patients had received, which included combination chemotherapies with or without rituximab—a monoclonal antibody that acts against B-cells.

"Over the last few years, people have realized that intrathecal CNS prophylaxis is probably inadequate, at least for diffuse large B-cell lymphomas, and many physicians have abandoned it," said Dr. Barta.

Dr. Barta, whose research focuses on ARL, said his findings suggest the approaches used to identify CNS involvement may be missing many patients who are at risk of CNS relapse, and current treatments are insufficient.

"A lot of patients who relapsed probably had undetected CNS involvement at diagnosis," he said. "We want to figure out if there are better strategies to identify patients at risk."

Provided by Fox Chase Cancer Center

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