

Epidemiology

Burkitt lymphoma is associated with malaria infection: study

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ATLANTA (Reuters Health) - Malaria may be associated with the development of Burkitt lymphoma as well as protection from it, researchers said here December 11 at ASH 2012, the annual meeting of the American Society of Hematology.

Endemic Burkitt lymphoma risk increases with greater exposure to Plasmodium falciparum malaria parasites, and antibodies due to antigens targeted by protective immunity might protect against endemic Burkitt lymphoma, they said.

"The role of malaria has been suspected for more than 50 years, based on a very close correlation between the incidence of endemic Burkitt lymphoma and the incidence of malaria. ... We think our results confirm the strong association between malaria infection and Burkitt lymphoma," said lead researcher Dr. Sam M. Mbulaiteye, of the Division of Cancer Epidemiology and Genetics at the National Cancer Institute.

The incidence of endemic Burkitt lymphoma is high in areas of endemic Plasmodium falciparum malaria, suggesting that malaria plays a role in endemic Burkitt lymphoma etiology.

Previous data indicate that children with endemic Burkitt lymphoma are five to 12 times more likely to have elevated antibody titers to a surrogate of exposure to malaria, the whole schizont extract, compared to controls of similar age and sex without the disease.

"My study investigated the relationship between antibodies to four antigens related to malaria and risk of Burkitt lymphoma. We measured these antibodies in the blood of children in Ghana where both malaria and Burkitt lymphoma are endemic," Dr. Mbulaiteye said in an email to Reuters Health.

The research team measured antibodies to serine repeat antigen 36 (SE 36), merozoite surface protein-1 (MSP-1), histidine-rich protein-II (HRP-II), and peptide 6NANP, plus antibodies to tetanus toxoid as an irrelevant antigen control.

Samples from the National Cancer Institute (NCI) Ghana Burkitt Lymphoma Study were used to study children aged 0-15 years enrolled at the Korle-Bu Teaching Hospital, Accra, Ghana, during 1965-1994. Controls were children enrolled at the same time from the same villages as the cases or children diagnosed with a benign or a non-hematologic malignancy.

"In each category, only one of the two antigens showed a statistical association with Burkitt lymphoma. We saw a significant increased risk in children who had the antibodies which indicate current or past infection with malaria. We also found a significant decreased risk in children with the antibodies associated with natural immunity to malaria," said Dr. Mbulaiteye.

The independent association of each malaria marker with endemic Burkitt lymphoma was determined by calculating the odds ratio and 95% confidence intervals (95% CIs).

Endemic Burkitt lymphoma was inversely associated with IgG1 seropositivity to SE36 (OR 0.54, 95% CI 0.34-0.86; $p=0.01$) and positively associated with HRPII (OR 1.47, 95% CI 1.06-2.02; $p=0.019$). The odds ratios for endemic Burkitt lymphoma were significantly decreased for low, medium, and high titers, but without a trend (0.44, 0.47, and 0.58 for low, medium, and high, respectively; $ptrend=0.216$).

Odds ratios increased significantly with increasing titers of IgG3 antibodies to HRPII (ORs 1.83, 1.91, to 2.25 for low, medium, and high titers, respectively; $ptrend<0.002$). Having antibodies to 6NANP was associated with endemic Burkitt lymphoma, but the confidence interval crossed 1 (OR 1.48, 95% CI 0.90-2.43).

"Our results provide further support for the hypothesis that malaria may be causally related to Burkitt lymphoma. Although our findings won't immediately help improve patient care, the results can direct future research into the prevention of Burkitt lymphoma....Two of the antigens are related to natural immunity to malaria infection and are now being investigated as candidates for a vaccine," said Dr. Mbulaiteye.

"Our results suggest that the risk of Burkitt lymphoma is associated both with childhood infection with malaria, and ineffective immune response to the infection. More studies are needed to understand the nature of this relationship, and the types and levels of antibodies that may be protective for Burkitt lymphoma," he noted.

"This is an example of an organism that can cause the disease and is associated with the development of the disease, but also if you mount enough immunity, protects you from the disease. That is very interesting," added Dr. Martin S. Tallman, chief of the Leukemia Service at Memorial Sloan-Kettering Cancer Center, New York, in an interview. Dr. Tallman was not involved with the study.

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