Four genetic variants ID'd for risk for progressive multifocal leukoencephalopathy

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Four genetic variants have been identified that are associated with an

increased risk for developing progressive multifocal leukoencephalopathy (PML), according to a study presented at the annual meeting of the American Neurological Association, held from Sept. 9 to 12 in Philadelphia.

Eli Hatchwell, M.D., Ph.D., from Population Bio UK Inc. in Begbroke, England, and colleagues examined genetic risk variants in PML patient genomes in a cohort of 336 patients with PML, 94 of whom had multiple sclerosis and were exposed to PML-linked drugs before developing PML.

The researchers validated four candidate PML risk genetic variants, which were associated with PML in population- and matched-controls. Carriers of at least one variant had a ninefold increased risk for PML in drug-exposed PML cases.

All four risk variants were predicted to be deleterious and were located in two immune pathways: the complement system (C8B, in the terminal pathway, and FCN2, in the lectin pathway) and genes causing or linked to hemophagocytic lymphohistiocytosis (HLH) disorders (STXBP2 and LY9). Two case reports have previously described patients with HLH who developed PML, underscoring this link.

"There are no treatments to cure PML, so prevention is the best defense, including knowing your genetic risk," Peggy S. Eis, Ph.D., from Population Bio Inc in New York City, said in a statement. "Even though the chance of developing PML is very low for some of these drugs, patients should still be screened given the ease and low cost of doing so relative to the avoidable potential consequences for those who do test positive."

More information: More Information