MPAN and PKAN serum biomarkers.

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Blood-based biomarkers represent significant progress in the clinical assessment of neurodegenerative diseases. Specific biomarkers of neuronal degeneration, such as amyloid-β, tau peptides, neurofilament light chain, β-synuclein, ubiquitin-C-terminal hydrolase-L1, and those of glial degeneration, such as glial fibrillary acidic protein, can measure key pathophysiological processes across various neurodegenerative diseases. In neurodegeneration with brain iron accumulation (NBIA), measuring synuclein pathology, and glial and neuronal degeneration, may provide important insights into the disease stage and can be used to monitor the disease and response to treatment.

To identify biomarkers that can serve as indicators of disease progression and treatment effectiveness, we enrolled 25 patients with genetically confirmed MPAN and 12 patients with PKAN, along with a control group of healthy volunteers matched for age and gender. Fasting serum was collected, frozen at -80°C, and stored until analysis. MMP-9, S100B, ICAM-1, E- and P-selectins, and total α-synuclein were measured using standard ELISA techniques according to the manufacturer's instructions. Serum levels of NfL, GFAP, Tau protein, and UCH-L1 were tested using the ultrasensitive ELISA method (SIMOA Quanterix).

MPAN patients exhibited higher serum levels of all biomarkers except BDNF. MMP-9, E-selectin, and P-selectin levels were 1.4 to 2 times higher than those in controls. S100B levels were ten times higher in MPAN patients, suggesting potential blood-brain barrier damage. Alpha-synuclein levels were 25 times higher, consistent with the accumulation of this protein in the brain. NfL, GFAP, and UCH-L1 levels were 8, 2, and 5 times higher, respectively. In PKAN patients, inflammatory biomarkers did not differ from controls. BDNF levels were reduced by approximately 30%, and alpha-synuclein levels were reduced by 50%. UCH-L1 and GFAP levels were not elevated compared to the control group, while NfL and Tau were significantly higher. MPAN and PKAN patients did not

differ in Tau and NfL levels. Although these diseases share similar clinical and radiological features, their differing pathology is reflected in the distinct serum biomarker patterns.