Peripheral blood inflammatory cytokines in isolated REM sleep behavior disorder

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A recent study on isolated REM sleep behavior disorder (iRBD) has revealed increased microglial activation in the substantia nigra along with reduced nigrostriatal dopaminergic function, providing insight into the role of neuroinflammation in iRBD.[1] However, the association of peripheral inflammation with iRBD remains unclear, although systemic inflammation is known to be related to brain inflammation and neurodegeneration.[2] Given the accessibility and practicality of using peripheral blood, measurement of inflammatory markers in serum or plasma may be an attractive option to study and monitor the immune response in iRBD. A recent study by Kim et al.[3] investigated plasma cytokine levels including interleukin (IL)-1β, IL-2, IL-6, IL-10, and tumor necrosis factor (TNF)-α and their associations with prodromal symptoms of α-synucleinopathies in 54 iRBD patients. The study did not find evidence for the role of peripheral inflammation in iRBD, but these results are limited by cross-sectional study design and the use of melatonin, which has anti-inflammatory properties,[4] in many participants included in the study.

In this prospective cohort study, we analyzed serum samples from patients with polysomnography-confirmed iRBD (*n*=30) and healthy controls (*n*=12). We measured the following cytokines: IL-1β, IL-2, IL-6, IL-10, and TNF-α. All patients underwent motor and non-motor evaluations and dopamine transporter imaging at baseline for predicting the

phenoconversion risk. We prospectively followed the patients quarterly a year over up to 6 years to identify disease conversion. We also assessed longitudinal changes in cytokine levels from baseline at the 2- and 4-year follow-up visits. The baseline cytokine levels did not differ between the patients and controls. However, the TNF-α levels were significantly increased in a subgroup of the patients with multiple markers (≥3) for phenoconversion risk compared to those without (p=0.008) and controls (p=0.003). At longitudinal analyses, patients with TNF-α levels above the median showed a higher incidence of phenoconversion than those with lower TNF-α levels (47% vs. 7%; p=0.008), and this significant association persisted after adjusting for covariates (p=0.026). The cytokine levels over 4 years of follow-up period did not change significantly. Our data suggest a possible link between serum TNF-α and phenoconversion risk in iRBD. Further studies are warranted to confirm the role of peripheral TNF-α in the pathogenesis of neurodegeneration in this disorder.

References

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