MULTIPLE SCLEROSIS

Persistent antibodies against IFN-β worsen MS progression

Neutralizing antibodies (NAbs) against interferon beta (IFN-β) persist after treatment withdrawal and are associated with an increase in relapse rate and faster disability progression in patients with multiple sclerosis (MS), according to findings from the VU University Medical Center in The Netherlands. "Persisting antibodies against IFN-β correlated with increased disease activity in MS patients long after treatment had been stopped. This was also reflected in the need for more-aggressive treatment in these patients," says researcher Laura van der Voort.

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MS is a chronic disease and a leading cause of disability in young adults. IFN-β therapy is extensively used as a first-line treatment for relapsing–remitting MS. However, long-term treatment with IFN-β is known to lead to an immune response against the recombinant protein in many cases. Previous studies have shown that anti-IFN-β NAbs can persist after treatment has been stopped and can influence the efficacy of the treatment. "We were fascinated by the fact that the body started to produce antibodies against IFN-β, a key player in regulation of immunity and inflammation. What would be the implications if such antibodies would persist? Would these patients be more likely to develop cancer, suffer from infections or increase of autoimmune disease activity?" adds van der Voort.

The research team restropectively examined the medical records of 71 patients with relapsing–remitting MS from the Multiple Sclerosis Center in Amsterdam to confirm whether NAbs to IFN-β could persist after treatment withdrawal, and to assess whether these persisting NAbs affected the progression of the disease.

The researchers found that 24% of patients tested positive for anti-IFN-β NAbs within a median interval of 25 months after termination of IFN-β therapy; 15% of these patients had high-titer levels of anti-IFN-β NAb. Patients treated with 22 μg or 44 μg subcutaneous IFN-β1a 3 times a week were more frequently positive for persisting NAbs than were patients treated weekly with IFN-β1b or intramuscular IFN-β1a.

The investigators also showed that persistent anti-IFN-β NAbs were associated with an increase in the annualized relapse rate and a reduction in time for MS progression. Finally, they found that NAb-positive patients were more likely to be treated with aggressive second-line therapy, especially mitoxantrone.

"Prospective studies with larger patient numbers should be performed to confirm [our] results. Our results imply that future treatment choices are to be influenced by the tendency of a patient to develop persisting NAbs," concludes van der Voort. She points out that this is one of the topics being addressed by a large European project, NABINMS (Neutralizing Antibodies on IFN-β in Multiple Sclerosis), which was initiated in 2006.

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