Lesions May Resurge After Halting Natalizumab

VITALS

Major Finding: Abrupt discontinuation of natalizumab coincided with a surge in gadolinium-enhancing lesions on MRI that mostly resolved by 9 months without any clinical deterioration.

Data Source: Case series of 11 patients who had received natalizumab infusions before abruptly discontinuing the therapy

Disclosures: Dr. Khan said the study was independently funded and he did not have any financial declarations to make.

BY MICHELE G. SULLIVAN

BANGKOK, THAILAND — Patients with multiple sclerosis who abruptly discontinue natalizumab treatment may develop a sudden surge in the number of gadolinium-enhancing lesions apparent on imaging, which seems to resolve by 9 months.

The phenomenon is probably a reaction to the sudden resurgence of lymphocytes into the brain—a central nervous system form of immune reconstitution inflammatory syndrome, Dr. Omar Khan said at the World Congress of Neurology.

Although the dramatic imaging changes aren't accompanied by clinical deterioration, about 22% of the lesions did develop into nonenhancing T1 hypointensities, said Dr. Khan, director of the Wayne State University Multiple Sclerosis Clinical Research Center and Radiology Image Analysis Laboratory, Detroit. "Some patients may accumulate a lot of irreversible neuronal damage in this short period of time. And although it's too soon to know for sure, my gut feeling is that over 3 or 4 years, there might be some consequences."

Dr. Khan presented a case series of 11 patients with MS who had received natalizumab infusions before stopping the treatment abruptly. The reasons for discontinuation included infusion site reactions, the development of neutralizing antibodies, changes in insurance coverage, and worries about developing progressive multifocal leukoencephalopathy.

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DR. KHAN

The patients' mean age was 36 years. They had undergone a mean of 13 natalizumab infusions, although that number ranged from 8 to 21. Before taking natalizumab, their mean relapse rate was 1.6/year; the mean relapse rate at discontinuation of the drug was 0.1/year. All patients were negative for John Cunningham (JC) virus.

Before beginning natalizumab, the patients had a mean of 12 T2 lesions, two T1 lesions and 20 gadolinium-enhancing lesions on MRI. Three months after stopping the drug, the numbers of lesions increased significantly, to 17 T2 lesions, 13 T1 lesions, and 137 gadolinium-enhancing lesions. Overall, 93 of the lesions appeared in brain areas that were previously normal-appearing on imaging.

Before natalizumab discontinuation, the mean magnetization transfer ratio value of the gadolinium-enhancing lesions was 31%; at month 3, the mean value had dropped to 19%. "This is a pretty impressive decline, something telling us there might be some fairly intense inflammatory injury on these sites," Dr. Khan said.

Despite the "alarming" scans, Dr. Khan said, the patients did not show corresponding clinical deterioration. Their mean Expanded Disability Status Scale (EDSS) was 3.2 at discontinuation and did not increase significantly by 3 months.

By 9 months, however, the scans had almost universally improved. The mean number of T2, T1, and gadolinium-enhancing lesions had dropped and were not significantly different from the number of lesions seen at baseline.

Clinically, the patients remained stable, Dr. Khan said. Their mean EDSS at 9 months was 4.0—not significantly worse than it was at natalizumab discontinuation. The mean relapse rate was also not significantly different. ■