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IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME IN NATALIZUMAB-ASSOCIATED PML

Kerstin Hellwig, Ingo Kleiter, Ralf Gold, Bochum, Germany: Tan et al.¹ postulated that early immunologic rebound in natalizumab-associated progressive multifocal leukoencephalopathy (PML) may implicate a worse outcome and survival. Unfortunately, the interval between the last natalizumab infusion and PLEX/IA was not provided.

Although it did not reach significance, the time between onset of symptoms and PML diagnosis was about 75% longer in those with early PML–immune reconstitution inflammatory syndrome (IRIS), which may contribute to a worse outcome. We treated 12 German PML cases and observed IRIS in all patients after PLEX/IA, but also a considerable extension of the PML lesions with development of new PML lesions in at least 4 patients. None of our 12 patients died, but one developed severe clinical deterioration and the MRI showed expanding PML lesions (without Gd enhancement in the first MRI). While IRIS seemed to be “controllable” in all our patients with repetitive pulses of corticosteroids, the only successful treatment of PML itself is to restore

immunocompetence, which is more easily achieved in natalizumab-PML than in the setting of HIV-associated PML.

Therefore, a clinical, immunologic, and radiologic risk stratification for development of severe IRIS or PML deterioration is necessary to determine if there are subgroups that may profit from PLEX/IA or those who may deteriorate. Prospective studies investigating the role of PLEX/IA in the subgroup of those with Gd enhancement at the time of PML diagnosis could be helpful.

Author Response: David B. Clifford, St. Louis; Eugene O. Major, Bethesda, MD: We agree with Hellwig et al. that prospective and critical analysis of the benefits and risks of PLEX/IA is highly desirable. The practical aspects of such investigations are extremely challenging, particularly because clinically significant inflammatory responses to PML are difficult to quantify, and are occurring in some cases even before contrast enhancement is detected on MRI scans. Consequently, it is not possible to know whether JC virus–driven oligodendrocyte lysis giving advancing PML or a damaging inflammatory response is causing progressive symptoms and changes on MRI scans. While the improved survival in PML cases in natalizumab-associated PML supports the current recommendations to routinely provide PLEX to remove natalizumab and activate immune surveillance in the brain, it would be very useful to develop the means to select populations where more gradual immune reconstitution might be preferred.

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CORRECTION

PRION-1 scales analysis supports use of functional outcome measures in prion disease

In the article “PRION-1 scales analysis supports use of functional outcome measures in prion disease” by S. Mead et al. (*Neurology*® 2011;77:1674–1683), there is an omission in the Acknowledgment. The authors also gratefully acknowledge the contribution of National Prion Clinic physicians Drs. Tom Webb, Suvankar Pal, and Durre Siddique. The authors regret the omission.

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Immune Reconstitution Inflammatory Syndrome in Natalizumab-Associated PML

Kerstin Hellwig, David B. Clifford, Ingo Kleiter, et al.

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