

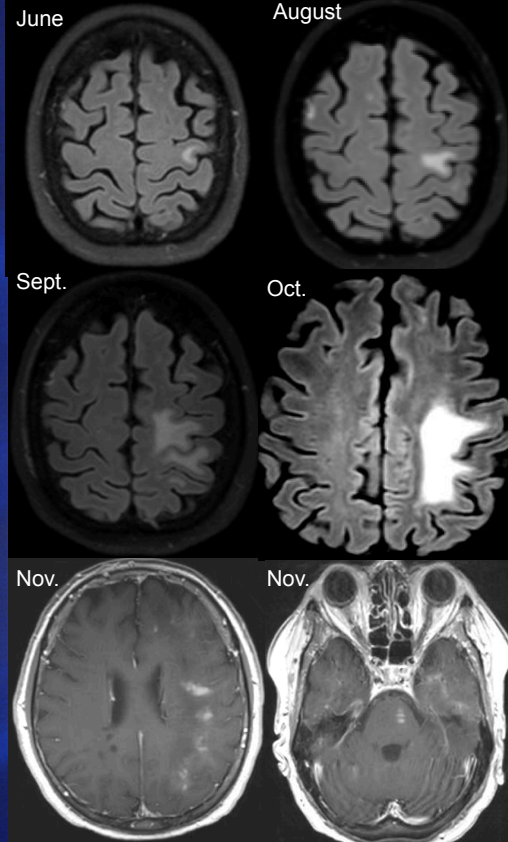
1: 10 000 Is Not Zero. Lessons Learned from a Natalizumab-Related PML Case with Repeated Negative Anti-JCV Antibody Testing



Marie-Sarah Gagné Brosseau, MD, Gary Stobbe, MD, Deb Cramer, RN, Hillary Lipe, ARNP, Annette Wundes, MD.
University of Washington, Seattle, Washington, USA

Introduction

- PML is the most feared complication of natalizumab.
- Seropositivity for anti-JCV Ab is an important risk factor, hence the rationale for periodic testing¹.



MRI		CLINICAL COURSE	TREATMENT
Brain MRI had been stable for years.	May 2014	MS course stable for years. EDSS 2.	-Tysabri infusion #55. -Anti-JCV Ab negative; index 0.19.
Routine annual MRI shows 4 new nonenhancing lesions. No evidence of PML.	June	MS center contacts patient: new mild right hand weakness and increased fatigue.	-Tysabri infusion #56. -3-day course of IVMP 1g die for presumed MS relapse.
	July	Right hand weakness progression.	2 nd 3-day course of IVMP 1g die.
Increase in non-enhancing FLAIR hyperintense lesion involving left precentral gyrus. Now extending in subcortical U fibers. Early PML not excluded.	August	Right hand now floppy with mild proximal weakness of right arm.	-Tysabri stopped. -PLEX + PML dx (PCR: 101 copies/mL). -Anti-JCV Ab +; index 2.56. -Trial of mirtazapine (stopped after 2 weeks due to drowsiness).
Progressive increase in size of confluent white matter lesion. No enhancement.	Sept.	Rapid progression of neurological impairment: right hemiparesis and speech impairment.	<div style="display: flex; justify-content: space-around;"> <div style="background-color: #f4a460; padding: 5px; text-align: center;"> IVMP: 3-day course every 2 to 4 weeks (for IRIS) </div> <div style="background-color: #e87633; padding: 5px; text-align: center;"> Mara-viroc (for IRIS) </div> </div>
Minimal enhancement (1 st time). PML lesions continue to sprawl.	Oct.	Reached nadir: right hemiplegia, global aphasia and severe apraxia.	
Enhancement at its zenith. PML lesions worse.	Nov.	Unchanged.	
Slight decrease in extent of PML lesions. Enhancement slowly decreases but persists.	Dec. - now	Mild amelioration of language, small non anti-gravity movements in right hemibody.	

Our case

- 70-yr woman with RRMS on natalizumab for > 4 years.
- Never received immunosuppressants.
- Developed PML symptoms 2 weeks after last negative anti-JCV Ab testing.
- Periodic testing for anti-JCV Ab every 3 months had always been negative.
- At time of diagnosis, serum anti-JCV Ab was positive with an index of 2.56.

Conclusion

- Previously, only 2 natalizumab-related PML cases were anti-JCV Ab negative but testing dated from 8 and 9 months before diagnosis¹.
- 2 weeks is the shortest interval ever reported between last negative anti-JCV Ab testing and PML symptoms onset.
- PML is a consideration in any natalizumab-treated patient with new MRI lesions or new symptoms and JCV antibody should be repeated even if recently negative.

References

1: Biogen Idec.Tysabri.